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THE RICKETTSIAL DISEASES

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Rickettsias are gram negative micro-organisms, coccoid or bacillary in form, found typically in arthropods. Those known to be pathogenic for man occur intracellularly in the tissues of their animal and arthropod hosts. These organisms have never been cultivated on artificial mediums free from living cells, but they grow and multiply in the various tissue culture mediums. With the exception of the rickettsia of Q fever, they do not pass filters that retain pathogenic bacteria. Several species that are not known to be associated with any disease of man or other animal have been described and named, and one species has been described that is pathogenic for lower animals but not, apparently, for man—this is Rickettsia ruminantium, the causative agent of "heart water disease" of sheep, goats and cattle; the identification of these organisms is based on appearance, staining reactions and occurrence in arthropods. Bodies resembling rickettsias have been isolated from cases of trachoma and psittacosis, and while there is not at the present time conclusive evidence on which to base the classification it is possible that further knowledge may place these bodies in the class Rickettsia.

The diseases of man with which species of Rickettsia are associated and of which the epidemiologic character is determined by the life cycles and the feeding habits of the arthropod vectors may be divided into four subdivisions: typhus, Rocky Mountain spotted fever, tsutsugamushi and Q fever. Q fever stands a little apart, differing somewhat from the other rickettsial diseases clinically and in the fact that the organisms readily pass through bacterial filters which retain the other strains of pathogenic rickettsias. Trench fever has often been classified as a rickettsial disease since it is louse borne and rickettsias have been described in lice and their feces which subsequently have infected volunteers. Opportunities for the careful study of trench fever have been lacking since it disappeared with the close of World War I. However, it has appeared in the European sector of the present war, and studies now in progress in Europe may clear up its relationship to rickettsias.

A characteristic of this group of diseases with the exception of Q fever is the production in patients of agglutinins for the X strains of Bacillus proteus (Proteus vulgaris). This agglutination of B. proteus X (Weil-Felix reaction) has been of great assistance in distinguishing the tsutsugamushi group from the typhus and spotted fever groups, since with tsutsugamushi agglutinins for the OXK strain of B. proteus are typically produced while the serums of patients with typhus and spotted fever agglutinate the OX_{19} and OX_2 strains. No strain of B. proteus has been found which is agglutinated by Q fever serums, and the production of agglutinins in trench fever is as yet unknown. There are definite immunologic differences, illustrated by absence of cross immunity, which separate the subdivisions of the rickettsial infections.

Clinically the typhus, spotted fever and tsutsugamushi groups are characterized by sudden onset, rash, fever of fairly well defined duration, mental disturbance and pronounced prostration.

The typhus subdivision of the rickettsial infections comprises the epidemic or louse borne type and the endemic, murine or flea borne type. The Rocky Mountain spotted fever subdivision is not so clearly delineated as yet but includes in addition to Rocky Mountain spotted fever other identical or similar tick borne diseases, such as boutonneuse fever, the misnamed São Paulo exanthematic typhus, Tobia fever of Colombia, Kenya typhus and possibly the so-called tick typhus of India and South African tick bite fever. The tsutsugamushi subdivision embraces, in addition to the type disease, the disease known as scrub typhus and other of the mite borne diseases of southern Asia and the islands of the Southwest Pacific.

Of the rickettsial diseases typhus is of greatest military importance. The Rocky Mountain spotted fever group is apparently not of much military significance, although cases have occurred in military personnel and the tsutsugamushi group is occurring to some extent among our troops in the southwest Pacific zone.

EPIDEMIC TYPHUS

Synonyms.—Spotted typhus, petechial fever, jail fever, ship fever, camp fever, typhus exanthematicus, fleckfieber (German), el tabardillo (Spanish), typhoesantematico (Italian).

Epidemic typhus is an acute infectious disease caused by Rickettsia prowazeki. The disease is characterized by a fairly sudden onset and a continuous fever of about two weeks terminating by crisis or rapid lysis. The most distinctive feature is a macular rash, which appears usually on the fifth or the sixth day. Persons of all ages and both sexes are susceptible.

History and Distribution.—Typhus has been one of the great pestilences of history. The earlier accounts of epidemics of diseases are not definite enough to allow the sure identification of any as typhus, but there is little doubt that, in 1489, 17,000 of the soldiers besieging Granada died of typhus. In the succeeding century a petechial fever, probably typhus, within a span of four years (1550-1554) destroyed 100,000 people in Tuscany. During the Thirty Years' War, 1619-1648, typhus repeatedly ravaged Europe. The disease appeared often in England and Ireland in the seventeenth, eighteenth and nineteenth centuries, Ireland

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becoming one of the principal endemic centers of the disease. The French Revolution, the Napoleonic wars, the Crimean War and the World War of 1914-1918 were all marked by typhus. At the close of the World War the disease was prevalent in Poland, Russia and Rumania, causing close to a million deaths in the last country. The estimates of typhus cases and deaths in Russia between 1919 and 1923 run into millions.

In the Western Hemisphere epidemic typhus appeared in Mexico shortly after the Spanish conquest. It appeared in South America following the Spanish conquest of Peru, and in the highlands of Central and South America it has since remained endemic. Typhus was brought to Canada in 1659 and several times in the eighteenth and nineteenth centuries. One of the first years of Irish immigration in great numbers into Canada was 1847, Ireland, as previously mentioned, being one of the endemic foci of the disease. Of 84,445 persons immigrating into Canada that year, 75,540 were Irish. Among these there were 30,265 who sickened with typhus; 5,293 died at sea, 8,012 at Quebec and 7,000 at Montreal, making a total of 20,305 deaths. Typhus was introduced also into the various seaports of the United States at various times during the eighteenth and nineteenth centuries. This form of typhus (louse borne) has never established an endemic focus in this country or in Canada. It is noteworthy that our Civil War is one of the few wars of any magnitude in which cases of typhus did not appear in great numbers.

At the present time epidemic typhus has definite endemic foci in the highlands of Central and South America, North Africa and some parts of Central and South Africa, in Spain, in parts of France and Germany and in the invaded states of East Europe, in Russia, Turkey, Iran and Iraq, in Afghanistan and in China. There has been a definite increase in epidemic typhus in the European and North African zones since the inception of the present war.

Transmission.—Epidemic typhus is transmitted from person to person by body lice. Rickettsias are present in the feces of typhus infected lice in great numbers, and it is probable that from deposits of such feces they gain entrance to the body through abrasions in the skin. The high morbidity rate among doctors and nurses in epidemics of typhus, coupled with the fact that as a group such persons are surrounded by careful precautions with regard to protection against lice, suggests that actual contact with lice may not always be necessary. It has been shown that rickettsias remain viable and retain their virulence for many days when in dried feces of lice, and since laboratory animals can readily be infected by intranasal inoculation and since the disease has developed in laboratory workers presumably after inhalation of infectious material it seems possible that the inhalation of dried infected louse feces or the deposition of air borne infected material on the mucous membranes may be responsible for some cases.

Epidemiology.—The chief epidemiologic characteristics of epidemic typhus are as follows:

1. It occurs among populations disorganized by war, famine and social revolution.
2. It occurs first and most commonly in the poorer sections of cities, in concentration camps and in prisons.
3. It is readily transmissible from person to person through the agency of the body louse.
4. It is associated with lousiness.
5. The peak of prevalence is in the winter and spring.

There is no difference in susceptibility conferred by sex. One attack usually confers immunity which may not be permanent. There is some evidence to indicate that the more severe the attack the more lasting is the subsequent immunity.

Clinical Features.—The incubation period falls between five and fifteen days; the usual time is eight to twelve days. The onset may be preceded by one or two days in which the patient experiences malaise, headache, loss of appetite and at times nausea. In the majority of cases the disease begins abruptly with rapidly rising fever, repeated chills (not often severe) and headache.

The fever rises steadily during succeeding days, usually reaching its maximum by the end of the first week. Morning remissions of fever occur. These remissions may be slight during the second week. The fever falls usually by rapid lysis after about fourteen days, patients with uncomplicated typhus ordinarily being afebrile by the sixteenth day after the onset.

Headache is a prominent symptom, being severe and difficult to relieve. It often persists throughout the illness and may be the chief symptom complained of by the patient. Prostration and signs of cardiac weakness may be evident from the onset, usually becoming pronounced by the second week of the illness. Constipation may be troublesome throughout the illness. The general features of prostration tending toward stupor and delirium become more grave in the second week. In severe disease with definite cardiac weakness there is a tendency toward development of gangrene of the extremities, more frequently of the toes. Mental disturbance is common. This may vary from confusion, disorientation, restlessness, insomnia and irritability to delirium. Generalized aching and soreness of the eye muscles are often present. Nosebleed sometimes occurs.

In cases of severe involvement which end in recovery there is often a sharp change toward the end of the second week. If the disease is uncomplicated the temperature falls and the stuporous condition disappears about the fourteenth day. Prostration and cardiac weakness continue for a varying length of time after defervescence, depending to a great extent on the age of the patient, those in the lower age groups recovering more quickly. In cases which proceed to a fatal outcome the prostration and the mental cloudiness increase, and coma occurs.

Some evidence of involvement of the respiratory system is usually present. This varies from a mild cough, which may never be troublesome, to definite bronchopneumonia.

The most characteristic feature of the disease is a rash which appears on the fourth to sixth day after onset of the illness. Rarely it may appear as early as the third or as late as the ninth day. The rash consists of rose red macules and papules. These lesions at first disappear on pressure but rapidly become petechial and darker as the disease progresses. In severe involvement coalescence of the lesions occurs. The eruption appears first on the inside surfaces of the upper arms or on the sides of the chest and the upper part of the abdomen and spreads to the rest of the chest, the back, the arms and the legs, usually being less pronounced on the extremities. The palms and the soles may be involved, while the neck and face are seldom included in the area of distribution. The

rash becomes brownish as recovery ensues, usually disappearing during defervescence. In some cases the remnants of the rash may be discernible for several weeks.

The pulse rate often remains below 120 or even 100. A rate of over 130 indicates severe involvement with a doubtful prognosis. Not uncommonly there is a drop to a rate lower than normal (50 to 60) during convalescence, the pulse gradually regaining the normal rate as strength returns. On recovery from a severe attack, shortness of breath may be noticeable for several weeks. Recovery once assured is usually complete and sequelae are absent.

The fatality rate varies from 20 to 60 per cent in different epidemics. In the same epidemic the rate may be below 5 per cent in children and over 80 per cent in those over 50 years of age. In sporadic cases in interepidemic periods the rate is much lower.

Complications.—Among the complications which may be encountered are bronchopneumonia, parotitis, otitis media, mastoiditis and thrombosis of various veins.

Laboratory Findings.—In many instances albuminuria is present at the height of the illness. It clears with convalescence.

Cytologic examination of the blood shows nothing characteristic. The white cell count varies from one indicating moderate leukopenia to one of about 12,000, with occasional uncomplicated cases showing as many as 15,000 white cells per cubic millimeter.

The Weil-Felix reaction usually becomes positive during the second week of illness, reaches its height about the time convalescence is established and disappears rather rapidly. It is advisable to test at least two samples of serum, one taken early in the illness and a second late in the second week. With a sensitive antigen the serums of patients with typhus often reach a titer between 1:10,000 and 1:100,000. The OX_{19} strain of B. proteus is more commonly agglutinated than OX_2 and is the strain customarily employed. The serums of patients with Rocky Mountain spotted fever also show the Weil-Felix reaction in high titers and consequently this reaction is of no practical value in differentiating between the two diseases. Serums from persons suffering from other illnesses not related to the rickettsial diseases may show the Weil-Felix reaction in dilutions as high as 1:320 and occasionally 1:640.

Recently it has been found that complement fixation can be utilized in the diagnosis of typhus. This test, with typhus rickettsias used as an antigen, becomes positive during the second week of the disease and may remain positive for many years. It is of value in differentiating typhus from Rocky Mountain spotted fever.

Pathology.—Grossly there is little else than the partially faded exanthem, moderate splenic enlargement and the frequent presence of complicating bronchopneumonia. The essential lesion is focal injury of capillary and precapillary vessels, characterized by endothelial swelling, proliferation and necrosis with thrombosis and by nodular perivascular exudation of lymphocytes, plasma cells and monocytes. Such lesions are most frequent in the skin, heart, great vessels, kidneys, adrenal glands, testes, epididymides and especially the brain, the cerebral cortex being usually the most involved. Very characteristic are small paracapillary nodes of microglia. Splenic hemorrhages, erythrophagia, plasma cell infiltration and infrequent thrombi are reported.

Treatment.—There is no specific treatment of established value. Convalescent human serums and serums from horses inoculated with rickettsias have been tried without convincing results. A hyperimmune rabbit serum has been described, and early results in a small series of cases indicate that it may be of therapeutic value. Many of the newer therapeutic chemicals have been tried, with little evidence of any value and some evidence of harm.

Good nursing with every care to maintain the strength of the patient is of the greatest importance. Cardiac depressants should be avoided. For the relief of the headache, acetylsalicylic acid may suffice; otherwise codeine or morphine may be necessary. Digitalis may be given with possible benefit to patients showing signs of cardiac failure. Constipation is best controlled by means of enemas or with mild laxatives. Care should be exercised to prevent bed sores. The patients, particularly those in the older age groups, should be confined to bed until convalescence is well established.

Prevention.—The prevention of epidemic typhus rests on the control of lice. All patients and their contacts must be completely freed of lice, and all persons coming from typhus-infected areas should be treated as contacts. The body louse nests in the clothing and usually remains there when the clothes are removed. Clothing may be disinfected by several methods using heat or pediculicide powders[1] and chemicals. The louse infested person should be bathed and the hair of the head and the body clipped. Those in attendance on patients (e. g. doctors, nurses and orderlies) should be provided with louse proof clothing made of white material and fashioned as coveralls with the openings at the wrist, ankle and neck closely fitted. Stockings should be drawn up over the bottoms of the coveralls and rubber gloves pulled over the wrists. Care should be taken in the examination of patients since there is some evidence that inhalation of the dried excreta of infected lice may be responsible for some secondary infections.

Vaccines of various types have been prepared for immunization against typhus. Attenuation of the living rickettsias by heat or by addition of such substances as bile, as well as partial neutralization by convalescent serum, has been used. However, the dangers inherent in the use of a vaccine containing living rickettsias as shown by the fact that attacks of the disease have been produced by inoculation with such vaccines should prohibit their use. Several preparations have been made which utilize rickettsias killed usually by solution of formaldehyde or phenol. One of them, that of Weigl, apparently gives good immunity, but unfortunately it cannot be produced on any very large scale, as its production requires that a suspension of rickettsias be injected into the rectums of lice, that the lice be subsequently fed on typhus immune persons and that the louse intestine be then removed and prepared as a treated suspension, which is used as the vaccine. Approximately one to two hundred lice are needed for the vaccination of a single person. A second source of rickettsias for the preparation of vaccine of killed organisms is the yolk sac of the developing chick embryo after its inoculation with typhus rickettsias. Vaccines made from killed rickettsias secured from the lungs of intranasally infected mice, rats or rabbits have also been prepared.

1. Evidence is accumulating that body lice can be controlled by the use of pediculicide powder alone.

The vaccines of killed rickettsias at present in use give good results when tested in animals, but no adequate field tests in the presence of epidemic typhus have as yet been made. Typhus has occurred in a number of laboratory workers who had previously received such vaccines and apparently was modified in severity, most of these workers showing very mild symptoms of only a few days duration. The length of time for which a vaccine may be expected to give its full protection is not known, but evidence at hand indicates that after the initial series of three injections a "booster" dose should be given every few months when the danger of typhus is present.

ENDEMIC TYPHUS

The difference between the epidemic form of typhus and the endemic or murine type is largely epidemiologic, with some variations, not entirely explained, in the immunologic observations and in the reactions produced by the infection in laboratory animals.

The causative organism of endemic typhus has been named Rickettsia mooseri, and the disease is also referred to as murine typhus and as Brill's disease.

History and Distribution.—Mild typhus was first reported in the United States in New York in 1898. In the next few years it was reported in additional communities—Atlanta, Ga., 1913; Charlotte, N. C., 1914; Galveston, Texas, 1916; Alabama, 1923, and others. The epidemiologic features indicated common rats as a reservoir, and typhus infected rat fleas and infected rats have been found many times in nature in foci where the disease was occurring in man.

In 1929 the human cases of endemic or murine typhus were practically limited to the towns, particularly those along the southern Atlantic coast from Baltimore south and continuing along the Gulf coast and up the Rio Grande River as far as El Paso, Texas, with a few cases in southern California. Towns in the interior of the Southern states were likewise affected but to a lesser extent as the distance from the seaboards increased. As late as 1932 the northern limit of the disease in Alabama was about in a line with Montgomery. Since 1932 cases have appeared farther north until at present the known northern limit of the disease has reached central Tennessee, with additional foci in Cleveland and Cincinnati and in Washington, D. C.

Since the identification of this form of typhus in the United States it has been found to be widespread over the world, especially along the sea coasts. It is probable that endemic typhus occurs at the inception of and during louse borne epidemics but is not recognized as such.

Transmission.—There is a reservoir of the infection in nature in the common rat and possibly in other rodents. Evidence indicates that the rickettsias are transmitted from rat to rat by rat fleas and rat lice. They have not been demonstrated in the salivary glands of the flea, and experiments to determine the transmission of this form of typhus by the bite of the flea alone have been unsuccessful. Transmission to man most probably occurs through the medium of the infected feces of rat fleas.

Epidemiology.—The chief epidemiologic characteristics of endemic typhus are as follows:

1. Human cases are associated with rat harbors.
2. The disease occurs most commonly among workers in food handling establishments.
3. There is no predominance of cases among the poorer sections of the population.
4. Transmission from person to person through contact or by rat fleas has not been observed.
5. The peak of prevalence is in late summer and fall.

Clinical Features.—The clinical features of the endemic form of typhus are identical with those of the epidemic form described earlier with the exception that in the average case they are much less severe than those in the majority of cases of epidemic typhus. The rash in endemic typhus does not often appear before the fifth day and may comprise only a few macules which may disappear in a day or so. The general symptoms are on the average much milder. The case fatality rate is below 5 per cent, with most of the deaths occurring in patients over 45 years of age.

The fact that the case fatality rate is much lower in murine typhus than in epidemic typhus has usually been considered to be due to a difference in the virulence of the flea borne as compared with the louse borne strains. It should be noted, however, that murine typhus occurs among populations in which the element of human distress is lacking, in contrast to the great epidemics of louse borne typhus which appear among the most miserable populations in time of war, economic depression, starvation, overcrowding and lack of heat. Murine typhus occurring under such conditions might possibly be a more severe disease. This question, together with that of the interrelationship of the two types of disease, remains to be answered.

The laboratory findings are similar to those noted for epidemic typhus except that leukopenia is more common. The Weil-Felix reaction is also positive in high titers.

When typhus is present as an epidemic, little difficulty should be experienced in making the diagnosis. Sporadic cases whether of the epidemic or of the endemic form of the disease give more difficulty. This is true particularly in those sections where cases of Rocky Mountain spotted fever or of tsutsugamushi may be encountered also. It is practically impossible to make a differential diagnosis prior to the appearance of the rash. Other diseases with which typhus has at times been confused are measles, meningococcemia and typhoid. Drug rashes also may be confusing.

Prevention.—The control of endemic typhus from present knowledge should be based on control of the rat population—by trapping, poisoning and rat proofing. The last of these measures is the only one that may be considered as of permanent value. Trapping and poisoning must be continuous to be of any practical value and must be supplemented with an attack on the rat's home and his sources of food by rat proof construction.

Vaccines are prepared against endemic typhus by the technics employed in the production of those for epidemic typhus. They have been shown to have good protective value in animals but have not been tested adequately in human beings.

ROCKY MOUNTAIN SPOTTED FEVER

The causative agent is Rickettsia rickettsii (Dermacentroxenus rickettsii).

History and Distribution.—As the name implies, Rocky Mountain spotted fever was first recognized in the Rocky Mountain section of the United States,

where it has been extensively studied since 1902. Until 1930 the disease was thought to be confined to eleven states of the Northwest although a case in Indiana had been reported in the literature and the diagnosis of spotted fever had been considered on occasion in other states prior to 1930. A recent review of clinical records shows that the disease was present in certain sections of the East at least as early as 1912. During the spring and early summer of 1930 the disease was clinically identified and the virus isolated in suspected cases occurring in the Eastern states. Since the time of definite identification of the disease in states outside the originally known area, new states or countries have been added to the known regions of distribution each year. At present study of suspected cases has shown that the area of distribution includes forty-one states. Five of the New England states—Maine, New Hampshire, Vermont, Connecticut and Rhode Island—have not as yet reported confirmed cases known to have originated in those states. In the Middle West, cases have not been identified in Wisconsin and Michigan. The number of cases reported each year in the United States has remained fairly constant: 560 in 1939, 457 in 1940, 516 in 1941. Rocky Mountain spotted fever is present in two provinces of western Canada and in two states of Brazil. In the latter country the disease has been named exanthematic typhus of São Paulo. It has been identified in Colombia, where it was originally described as Tobia fever.

Transmission.—Several species of ticks are known to be capable of transmitting Rocky Mountain spotted fever. Amblyomma cajennense, Dermacentor parumapterus marginatus, Dermacentor occidentalis, Rhipicephalus sanguineus and Dermacentor albipictus have been shown to be efficient transmitting agents under experimental conditions. However, the dog tick (Dermacentor variabilis), its near relative the wood tick of the Northwest (Dermacentor andersoni) and Amblyomma americanum are the only species biting man in which the virus of the disease has been found naturally present in the United States. Amblyomma cajennense is the common vector in Brazil. The rabbit tick (Haemaphysalis leporis palustris) has been found naturally infected, but this species does not bite man; it may, however, play an important part in preserving and spreading the virus in nature. There is no evidence at present to indicate that any arthropod other than the tick transmits the disease.

Clinical Features.—In many of its general aspects this disease resembles typhus, the chief differential points being the duration of fever and the time of appearance and the location of the rash.

In man the disease has an incubation period of two to twelve days, being most often a week or a little less. As in typhus, the actual onset may be preceded by a few days of ill defined prodromes—loss of appetite, listlessness and headache. The onset is usually sudden, with a chill or chilly sensations and rapidly rising fever. Prostration is usually pronounced. In the more severe type of the disease nosebleed may occur early. Soreness of the muscles and the joints is commonly present. The temperature rises rapidly, reaching its highest point usually in the second week. Morning remissions of 1 to 3 degrees F. occur. The termination of fever is by rapid lysis occurring usually about the twenty-first day, although patients with mild disease may be afebrile before the end of the second week.

The most distinguishing characteristic of the disease is the rash. This appears between the second and fifth days, usually on the third or the fourth. The typical rash may be preceded by a suggestive mottling of the skin, and this may easily be confused with the early rash of measles. The early rash usually disappears in a few hours to be followed by the typical maculopapular lesions. The lesions are rose red at first and become fainter, almost disappearing during the morning remissions of fever early in the disease. They become more distinct each day until they are definitely petechial in all but the mildest forms of infection. In severe involvement the spots become deep red or purplish and confluent. Necroses may develop. The rash usually persists throughout the febrile period and into convalescence, becoming brownish. Often a branny desquamation occurs over the areas where the rash was thickest. The site of first appearance and the spread and final distribution of the rash are important in the diagnosis of the disease. Usually the rash appears first on the wrists and the ankles, spreading rapidly in the first twenty-four to forty-eight hours to the back, then to the arms, the legs and the chest, and last to the abdomen, where it is least pronounced. The palms and the soles are frequently involved, often the face and occasionally even the scalp.

Nervous and mental symptoms are common: restlessness, insomnia, disorientation and in severe cases delirium. In fatal cases coma usually precedes death, which occurs about the end of the second week.

Convalescence of patients with severe involvement is apt to be slow and may be complicated by visual disturbances, deafness or mental confusion. Although recovery may be delayed, it is usually complete in the end. The case fatality rate, as in typhus, varies directly with age. The crude rate for reported cases in the United States is 18.4 per cent.

Laboratory Findings.—The white cell count is increased in cases of Rocky Mountain spotted fever, usually being about 12,000, although it may be as high as 30,000, which is in contrast to the count suggesting moderate leukopenia or the normal one usually seen in cases of typhus.

The Weil-Felix reaction gives no aid in differentiating spotted fever from typhus. In a large number of cases it has been noted that agglutinins for B. proteus OX_2 occur more frequently in the serums of patients with spotted fever than in those of patients with typhus, but since they do occur in some of the latter the stated difference is of no help in the individual case. When agglutinins for both strains are present, those for OX_{19} are usually higher than those for OX_2. The agglutinins for OX_{19} usually appear toward the end of the second week of the disease. At times they are delayed until early convalescence. In some proved cases of spotted fever no agglutinins for B. proteus X were produced. The curve of agglutinins in its rise and fall is similar to that seen in typhus. As in typhus, it has been found that complement fixation with the rickettsias of spotted fever used as an antigen becomes positive in the second week of illness.

Pathology.—Histologic changes in the brains of infected guinea pigs do not vary appreciably from those already described for typhus as far as the character of the individual lesions is concerned. It has been shown, however, that a higher proportion of the focal lesions

is found in the midbrain, pons, medulla and cerebellum in spotted fever than in typhus.

Treatment.—As with the other rickettsial diseases, there is no specific treatment of proved value. Injections of serum from convalescent patients have been tried repeatedly, as have transfusions from immune donors, but without definite benefit. A hyperimmune rabbit serum has recently been developed which has definite therapeutic value in the treatment of animals that are ill with spotted fever. A small series of patients has been treated with this serum with results indicating that this means of treatment will effect a reduction of the case fatality rate if the serum is administered before the third day of the rash. A definite opinion of its value should be withheld until additional observations have been reported. The newer chemicals—metaphen, sulfanilamide and sulfapyridine—have been tried clinically without definite evidence of benefit to the patient. The experimental use of sulfanilamide and sulfapyridine in the treatment of spotted fever in guinea pigs increases both the severity of the infection and the death rate.

Good nursing care, avoidance of exertion, mental or physical, maintenance of the fluid intake, by mouth preferably, by rectal drip or hypodermoclysis if necessary, and relief of the headache with acetylsalicylic acid, codeine or morphine give the best results. The mind of the physician may be relieved by the knowledge that there is more danger from overtreatment of these patients than from undertreatment.

In fatal cases death usually occurs before the fifteenth day, commonly between the eighth and the twelfth day. If the patient is going to recover, some indication of this may often be found in a slight decrease of the temperature about the fourteenth or fifteenth day which becomes more definite with each succeeding day. Final defervescence occurs by rapid lysis which often brings the temperature to normal about the end of the third week. The temperature may rise above normal in the afternoons for a few days longer. If no complications are present, a slow but steady improvement may be expected. After severe infections convalescence may be prolonged for many months, and remnants of the rash may be present for several months or even years.

Prevention.—Methods for the control of spotted fever have been directed toward the eradication of ticks but have not been very successful. The difficulties of the problem may be recognized when the variety of hosts on which these parasites feed is considered. Poisoning of rodents, dipping of domestic stock, clearing away of brush and burning over of tick infested areas probably assist in the reduction of ticks, but it is only fair to state that, although such methods have been tried, there is little evidence that much has been accomplished in the way of limiting the disease. Tick repellent powders have been tried, but the practical value of those in use is limited.

Probably the most effective method of prevention is the exercise of personal care. Known infected areas should be avoided as far as possible during the tick season. Those who must visit such areas should frequently examine clothing and body for ticks. Usually the tick does not become attached to its host at once but crawls around for several hours. It has been shown also that the chance of receiving infection from the bite of an infected tick is directly proportional to the length of time the tick has fed. Care should be taken in handling the tick when removing it from the person or from a pet. It is best to remove ticks with small forceps or with a piece of paper held in the fingers. The hands should be washed thoroughly with soap and water after handling ticks. Pets should be thoroughly deticked every few days during the tick season. There is little danger of leaving the mouth parts of the tick in the wound. The wound itself may be treated as any other abrasion, since there is nothing to distinguish the bite of an infected tick from that of a noninfected tick, nor is there any evidence that such measures as cauterization will lessen the chances of subsequent development of the disease.

A vaccine made from infected ticks for use against spotted fever was elaborated and is prepared by the United States Public Health Service at Hamilton, Mont. A second method of preparing vaccine is now in use. This method utilizes the rickettsias grown in the yolk sac of the developing chick embryo. Evidence from animal experiments indicates that the yolk sac and tick vaccines are of comparable value in prevention. Occasionally typhus occurs among those who have been vaccinated but is usually mild. The evidence as to total prevention is hard to evaluate but seems to indicate that vaccination appreciably lessens the chance of subsequent infection. There is no good evidence that the vaccine is of value after the infection has been acquired, nor is it of any value in treatment.

BOUTONNEUSE

Synonyms: Marseilles fever; fièvre exanthématique; escarro-nodulaire.

Boutonneuse is caused by Rickettsia conori and is closely related to Rocky Mountain spotted fever. It has an extensive distribution in Rumania, Portugal and the countries bordering the Mediterranean. Results of investigations indicate that the so-called Kenya typhus in East Africa and South African tick fever may be closely related to boutonneuse, the former probably being identical with boutonneuse.

Transmission.—The infection is transmitted by the brown dog tick Rhipicephalus sanguineus. As in some other rickettsial diseases, a reservoir probably exists in nature in the lower animals. The dog apparently is an important reservoir of boutonneuse. The tick R. sanguineus is also capable of harboring and transmitting the rickettsias of Rocky Mountain spotted fever.

Clinical Features.—The incubation period is five to seven days, although in occasional cases it may be as long as eighteen days.

As in other rickettsial infections, the onset is usually abrupt, with fever and repeated chills or chilliness. The temperature rises rapidly and may reach 104 F. in a few hours. Headache and pain in the muscles and the joints are common complaints. Prostration is usually not a prominent feature of this disease. The febrile period is from eight to fourteen days, defervescence taking place by rapid lysis.

Insomnia is common throughout the febrile period. As the disease is seen in Marseilles and Italy, mental disturbance is less severe than in other rickettsial infections, although patients with severe involvement may show moderate delirium. The case fatality rate is low, being less than 3 per cent.

A papular or maculopapular rash appears on the second to fourth day of illness. It begins on the trunk,

legs and arms and extends rapidly over the entire body, usually appearing on the face last. The palms and the soles are commonly involved. The rash may be less pronounced on the abdomen than elsewhere. It may be found on the soft palate as small round red spots which persist only a few days.

The individual lesions comprising the rash may become hemorrhagic, especially those on the legs, but there is little tendency to coalescence. The rash usually disappears with convalescence.

Frequently a small ulcer about 2 to 5 mm. in diameter, showing a black necrotic center surrounded by a red areola, is found at the onset of illness. This has been named tache noire (black spot) and is similar in appearance to the ulcer often seen in tsutsugamushi. The tache noire may be found on any part of the body, usually on a part covered by clothing; this is supposed to be the site of the infecting tick bite. Sometimes the regional lymph nodes become enlarged and tender.

The Weil-Felix reaction with the OX_{19} strain of B proteus used as an antigen becomes positive late in the disease.

Treatment and Prevention.—There is no specific treatment for boutonneuse, and no vaccine is available at present.

The prevention lies largely in the measures advised for the prevention of Rocky Mountain spotted fever.

TSUTSUGAMUSHI

Synonyms.—Japanese river fever; kedani fever; Japanese flood fever; scrub typhus.

Tsutsugamushi is an acute febrile disease clinically resembling the other rickettsial infections. The causative organism is Rickettsia nipponica (Rickettsia orientalis, Rickettsia tsutsugamushi). The disease has long been recognized as prevailing in Japan along the course of rivers and has shown a tendency to increase at the time of flood conditions. Originally thought to be confined to Japan, it has been shown to be probably identical with the so-called scrub typhus of Malaya, the mite borne coastal fever of Queensland in Australia and the pseudotyphus of Sumatra. It is also present in the Philippines and probably has a fairly wide distribution throughout the other islands of the southwest Pacific.

Transmission.—Tsutsugamushi is transmitted to man from a reservoir probably in field mice and other rodents by the larval form of the mite Trombicula akamushi or kedani mite. In Malaya and Sumatra the transmitting mite is named Trombicula deliensis. The larvae of this mite do not ordinarily feed a second time, and the adults do not feed on animals. The infection contracted by larvae through feeding on infected rodents is apparently transmitted through subsequent stages of the life cycle to the larvae of the next generation.

Epidemiology.—In Japan the disease is more prevalent during the summer months, while in Malaya there is little seasonal variation. There is a greater incidence of the disease among males than among females, a fact that is explained by the occupational exposure of males in rural occupations.

Clinical Features.—The incubation period in a small series of cases was determined as seven to twenty-one days, the common period being a little less than two weeks. As in the other rickettsial diseases, prodromal symptoms such as headache, malaise and loss of appetite may precede the onset. At the onset chills or chilliness, headache and fever occur. Deafness is not an uncommon early symptom and may persist throughout the disease. There may be pain in the joints and in the chest. Drowsiness or some other evidence of mental disturbance is often present. The fever is continuous in type with morning remissions of 1 to 3 degrees (F.). Prostration is often noted throughout the illness. In patients who are recovering the temperature usually falls to normal about the fourteenth to sixteenth day. This may be followed by a slight rise in temperature on the succeeding day or days to be followed by complete recovery. The case fatality rate for all ages is about 15 per cent. A definite increase of the rate occurs with increase of age.

The most characteristic sign consists of a small necrotic ulcer supposedly at the site of the infecting mite bite. This ulcer is 2 to 5 mm. in diameter with a black necrotic center surrounded by a red areola. Apparently it is found in the great majority of cases of tsutsugamushi as observed in Japan. In the disease as it occurs under the name of scrub typhus in Malaya the initial ulcer is not always present. There is general lymphadenopathy; which is especially noticeable in glands draining the site of the primary ulcer, which is usually found in the pubic region, in the axilla or on the legs.

The characteristic rash of tsutsugamushi appears from the fourth to the eighth day after onset and consists of macules and slightly elevated rose red or pink papules; it does not become petechial. This rash appears first on the trunk and the face and extends to the legs and the arms. It may be present on the palms and the soles, and occasionally the face and the scalp are involved. The rash reaches its height in about four days and fades within six or seven days. An enanthem may be present on the soft palate.

Many of the patients show bronchial symptoms with a dry cough; in occasional ones a mucopurulent sputum develops and pneumonia may occur as a complication.

Hyperesthesia, pains in the muscles and the joints, deafness, clouded mentality, insomnia and delirium may be encountered. A certain degree of immunity is conferred by an attack, but in some cases this lacks permanence.

The Weil-Felix reaction with the OXK strain of B. proteus used as an antigen is usually positive after the tenth day in dilutions of 1:160 and above, but not that with the OX_{19} or that with the OX_2 strain. The waxing and waning of the patient's agglutinins against the OXK strain of B. proteus is similar to that seen in tests with strains OX_{19} and OX_2 in cases of typhus, the peak titer being reached about the time convalescence is established. In some cases the Weil-Felix reaction may remain persistently negative. As in other rickettsial infections, it is advisable to examine one sample of serum when the disease is first suspected and a second sample near the termination of illness.

Pathology.—Microscopic examination of the brain shows the presence of lesions similar to those found in Rocky Mountain spotted fever and typhus.

Treatment.—There is no specific treatment for tsutsugamushi. Drugs may be used, especially to relieve headache and insomnia. As in other rickettsial diseases, cardiac depressants should be avoided. The

primary ulcer may be treated like any other similar lesion of the skin as there is no evidence that local treatment of the ulcer will influence the course of the disease once it has developed.

Prevention.—The wearing of mite proof clothing has been recommended by the Japanese for those working in mite infested regions. Since many of these areas lie in the tropics it is doubtful that this recommendation is of much practical value. Repellent powders, shown to be of value against lice, may be tried. Frequent baths may be of some value in removing mites prior to attachment for feeding. When possible the bed should be made on some structure which will remove the bedding from contact with the ground.

No vaccine has been developed against tsutsugamushi. Since there is no cross immunity between this and the other subdivisions of the rickettsial diseases, it is not to be expected that vaccines against typhus and spotted fever will be of any value against tsutsugamushi.

Q. FEVER

Present knowledge of Q fever began in 1937, when human cases of this new disease entity were described in Australia and shown to be caused by an organism to which the name Rickettsia burneti was given. At about the same time a strain of rickettsias was isolated from ticks in Montana and named Rickettsia diaporica. Later work showed that these two infectious agents are identical. R. burneti has been isolated from ticks and from bandicoots in Australia. The rickettsia of Q fever differs from the other known pathogenic strains of rickettsias in being readily filtrable through ordinary bacterial filters. Agglutinins for the X strains of B. proteus do not develop in the serum of patients with this disease.

Q fever may appear in two clinical forms, one presumably transmitted by the tick and the other probably air borne from infected animals or possibly from the dried feces of infected ticks. This second form of the disease has been recognized only in accidentally infected laboratory workers.

The Australian cases have been in general confined to workers in abattoirs, to foresters and to dairy workers.

Clinically the cases reported in Australia are characterized by a fairly acute onset with chills, prostration and fever. No rash appears. Headache is pronounced in the majority of cases; sweats at night and insomnia are common. The fever is continuous in type, lasting from a few days to two to three weeks. The pulse is slow in comparison with the height of the temperature, and the white blood cells remain within normal limits. Neither symptoms nor thoracic findings in the Australian cases have suggested any important pulmonary involvement.

The disease in the laboratory workers accidentally infected, referred to in a foregoing paragraph, belonged clinically in the atypical or virus pneumonia group. In these patients two types of onset predominated, one coryza-like, the other with headache, chilly sensations and general malaise. Following the onset there was a latent period of about three days in which the patient continued to work while feeling ill. One laboratory worker had a dramatic onset with abdominal cramps, chills, fever and headache while at work.

Severe and persistent headache was an outstanding symptom developing during the latent period. Other complaints on admission to the hospital were chills, fever, sweats and generalized body aches and pains. A few of the patients had experienced some nausea and vomiting earlier. A short hacking cough developed in several of the patients. In only a few was this cough productive, with a small amount of thick tenacious white mucus. In none of the cases was there observed a "prune juice," "rusty" or blood tinged sputum. In approximately half of the cases vague pains developed in the substernal region or on the side of the demonstrated pulmonary lesion. The pain in the chest had more the character of neuralgia than of pleurisy, as it was not associated with respiration. All the patients complained of insomnia.

Roentgen examination of the chest gave the most typical and consistent evidence of pulmonary lesions. Soft, infiltrative lesions, single or multiple, were visible on the films but were not of the uniform density seen in lobar pneumonia, these lesions appearing to be more of the patchy type observed in bronchopneumonia. The roentgenologist reported the films as revealing early pneumonia or pneumonitis.

Physical signs of pulmonary involvement were minimal. A slight dulness to the percussion note, a slight increase in breath sounds of a bronchovesicular character and an occasional moist rale over the involved area were the most that usually could be elicited. It is doubtful if without roentgen examination many of these patients would have been seriously considered to have had a pneumonic process.

Although the disease in these cases closely followed the picture presented by the so-called atypical pneumonias, efforts to isolate R. burneti from other atypical pneumonias has so far resulted in failure.

Treatment is symptomatic.

The case fatality rate in both forms of Q fever is practically zero. The disability lasts from ten days to three or four weeks.

TRENCH FEVER

Trench fever, also known as five day fever and Wolhynian fever, is a febrile disease transmitted to man by the body louse. Extracellular rickettsias have been found in lice fed on patients with the disease and are present in the feces of such lice. Trench fever disappeared after World War I and opportunity was not present for intensive study until its recurrence with the present war. As a result its true relationship to the other rickettsial infections is not yet known.

The incubation period varies from five to twenty days. The onset is sudden with headache and pain in the legs, most noticeable in the shins. There is a sharp rise in the temperature which may endure for about five days to one week, to be followed by a normal temperature. Relapses are frequent, three or four recurrent bouts of fever being common.

A rash is present in the majority of cases, being usually macular, with occasional cases showing papules. This rash may occur as early as the second day of the initial attack of fever or during one of the relapses. It is most commonly observed on the trunk and may disappear in twenty-four hours.

There is no report of agglutination of any of the X strains of B. proteus by serums from patients.

The death rate is nil.

There is no specific treatment for this disease and no vaccine. Prevention, as in epidemic typhus, consists in the eradication of body lice.

THE ACUTE DIARRHEAL DISEASES

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Historically the diarrheal diseases have been a plague of armies, a major hazard to the life and health of infants and a common cause of illness among institutional inmates. The expanded sphere of our nation's activity now includes areas where these disorders still remain in their historical place of importance. Thus American physicians and health authorities face the acute diarrheal diseases not as a fast disappearing group of disorders but as a major current medical problem.

During the past six years the National Institute of Health has maintained a field laboratory for the investigation of these diseases. Studies have been conducted in four widely differing areas selected as representative of those with very high, high, medium and low mortality from diarrheal diseases (Puerto Rico, New Mexico, Georgia and New York City). As a part of this work we studied 1,499 cases occurring in the general population, obtained satisfactory clinical data on 1,247 of these and recorded epidemiologic histories on 830 households. A total of 8,643 survey fecal cultures were obtained on representative persons. Institutional inmates, among whom clinical disease and subclinical infection were relatively common, have been studied extensively, and some observations were obtained on military groups in which diarrheal disease was troublesome. New, highly selective culture mediums were used which increased the reliability of bacteriologic findings.

ETIOLOGY

A clinical and etiologic classification of the diarrheal diseases is given in table 1. Primary infectious diarrhea is caused by pathogens which establish themselves and grow in the enteric tract. Various organisms are known to be responsible, and others are held under suspicion. In parenteral and secondary diarrhea the gastrointestinal disturbance is but one part of a symptom complex. The genesis of the diarrhea that frequently occurs in acute infectious diseases, in paranasal sinusitis and in some other localized infections is not clearly known.

Acute noninfectious diarrhea is commonly caused by the ingestion of toxic or irritating substances. The offending material is usually food in which staphylococci or other organisms have grown. Water heavily polluted with bacterial decomposition products or industrial wastes is involved less frequently. Allergic and neuropsychiatric disorders as well as nutritional deficiencies may cause episodes of diarrhea, usually chronic in form. The popularly incriminated "dietary indiscretion" is blamed rightly in some cases. Various chemical compounds, including cathartics, also may give a noninfectious diarrhea.

A classification of "cause unknown" has weight only following adequate study by competent observers. Some cases may be differentiated as instances of infectious or of noninfectious diarrhea through their clinical and epidemiologic characteristics.

Having in mind the causes of diarrhea, the first problem in an etiologic study is to determine the relative importance of each. In this report we limit attention to the acute diarrheal diseases. Cholera with its distinctive clinical features and limited geographic distribution will not be considered.

The proportion of patients with endemic diarrheal disease whose stools were found culturally positive for Shigella in our study is given in table 2. The findings in New Mexico and Georgia were similar, and the data from these states are shown combined. The stools of the patients were examined culturally at least once during the acute phase of the disease. The fecal specimens from 76 per cent of those with severe and 58 per cent of those with milder disease were culturally positive for Shigella. There was an increase in the proportion of those with positive fecal cultures as the number of examinations during illness increased—from 62 per cent of those with severe disease who had one examination to 90 per cent of those with more than three examinations. The stools of a few of the New York City patients were examined late in the illness, but all the patients are included. The proportion whose disease was found due to Shigella was less than in New Mexico and Georgia.

The percentage with positive findings was lowest for the group whose ages were under 6 months, but the percentage varied widely with area and with severity of illness. In New Mexico and Georgia 63 per cent of the infants under 6 months with severe diarrheal disease had cultures positive for Shigella; 33 per cent of those with mild intestinal disorder had positive cultures. In New York only 7 per cent of the 57 patients under 6 months were found to have positive cultures. Corresponding variations, though less pronounced, are apparent in the groups with ages from 6 to 12 months and at one year. In older age groups the percentage with positive findings was high in all three areas.

The cultural findings for institutional inmates were of a similar nature. At a hospital for patients with mental diseases in Puerto Rico, for example, 149 (75 per cent) of a total of 198 patients reported as having diarrhea were found to have fecal cultures positive for Shigella.

Each clinical case of acute diarrhea observed in New Mexico during the first two years of our study was examined by an experienced protozoologist (the late Bertha Kaplan Spector), but in spite of a carrier rate of 19.4 per cent a diagnosis of amebic dysentery was confirmed in only 1 case, whereas the common occurrence of bacillary dysentery was readily established.

Salmonella was rarely isolated from persons with endemic disease.[1] This is in sharp contrast to observations reported from South America.[2] Workers in Montevideo, Uruguay, studied bacteriologically 395 infants and children hospitalized for "enteritis." They isolated Salmonella from 126 (32 per cent) and Shigella from 80 (20 per cent).

Various strains of paracolon bacilli, of Pseudomonas (e. g. Bacillus pyocyaneus) and of Proteus were isolated from patients whose stools were otherwise culturally negative. They were also found in the stools of healthy persons. Our data did not establish or

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1. In a study now in progress in New Orleans these organisms have been isolated from more than 10 per cent of the children hospitalized for diarrheal disorders.

2. Bonaba, J.; Carrau, A.; Hormaeche, E., and Zubino, V.: Estudios sobre la etiologia infecciosa de las diarreas infantiles, Montevideo, Editorial Médica, J. Garcia Morales, 1940.

disprove the etiologic role of these organisms. Parasitologic examinations were obtained in the New Mexico cases. Intestinal parasites did not appear to be responsible for any of these.

Parenteral infection was of minor importance as a cause of acute diarrhea in New Mexico, Georgia and Puerto Rico; it was believed responsible in a relatively high proportion of the cases in which the stools were culturally negative in New York.

groups and 10 among the inmates of hospitals for patients with mental diseases) were nonexplosive in character. All these were found due to some variety of S. paradysenteriae. There were 9 explosive epidemics. One of these was due to Shigella and another to Salmonella typhi murium. In 7 the stools of all persons examined were culturally negative for these organisms and the outbreaks had the clinical and epidemiologic features of "food poisoning."

TABLE 1.—*A Clinical and Etiologic Classification of Diarrheal Diseases*

Group	Clinical Entities	Usual Course	Severity	Etiologic Agent
Primary infectious diarrhea	Bacillary dysentery	Acute	Mild to very severe	Shigella dysenteriae and Shigella paradysenteriae, varieties Shiga, Flexner, Sonne, Newcastle (Boyds 88) and Schmitz
	Amebic dysentery	Acute to chronic	Severe	Endamoeba histolytica
	"Food infection"	Very acute	Severe	Salmonella, chiefly S. typhi murium and S. enteritidis
	Cholera	Very acute	Very severe	Cholera vibrio
	Other bacterial infections	Variable	Mild	Slow lactose fermenting paracolon bacilli and pseudomonads are under suspicion
	Parasitic diseases	Variable	Variable	Various helminths and flagellates
Parenteral and secondary diarrhea	Parenteral diarrhea	Acute	Moderate to severe	Chiefly streptococci, also staphylococci and pneumococci, possibly viruses
	Tuberculous enteritis	Chronic	Severe	Tubercle bacilli
	Generalized infections	Variable	Variable	Variable
Noninfectious diarrhea	"Food poisoning"	Acute	Moderate to severe	Toxin producing staphylococci and possibly other organisms
	"Sewage poisoning"	Acute	Mild to moderate	Products of bacterial decomposition
	Nutritional diarrhea	Subacute	Mild	Dietary deficiency and "insults" to gastrointesteinal tract
	Allergic diseases	Acute to chronic	Variable	Variable
	Neuropsychiatric disorders	Chronic	Variable	Variable
	Other	Chronic	Severe	Local ulcerative or obstructive lesions such as those due to neoplasm and lymphogranuloma venereum
Diarrhea of unknown cause	"Epidemic diarrhea of newborn" *	Acute	Severe	Unknown

* Illustrative of various entities of unknown cause.

TABLE 2.—*The Cultural Findings for Shigella Paradysenteriae in Endemic Diarrheal Disorders*

	Cases in New Mexico and Georgia *						Cases in New York City †		
	Severe Disease			Milder Disease					
Age Group	Number in Which Fecal Cultures Were Made	Positive		Number in Which Fecal Cultures Were Made	Positive		Number in Which Fecal Cultures Were Made	Positive	
		Number	Per Cent		Number	Per Cent		Number	Per Cent
Under 6 months	41	26	63	27	9	33	57	4	7
6-12 months	45	31	69	44	23	52	21	4	19
1 year	55	43	78	56	37	66	27	9	33
2- 4 years	30	28	93	61	42	69	38	26	68
5-14 years	9	9	100	22	15	68	37	28	76
15-44 years	49	37	76	43	25	58	7	5	71
45 years and over	18	12	66	11	2	18	3	2	67
Unknown	2	2	100	4	2	50	1	0	0
Total	249	188	76	308	155	58	191	78	41

* In these cases the stools were first culturally examined during the acute phase of illness.
† In most of these cases fecal cultures were first made during the acute phase of illness.

The endemic disorders seen by us rarely had the character and the course of diarrheal disorders due to ingestion of toxic or irritating substances. Occasional household outbreaks could be classified as "food poisoning."

Our study of endemic diarrheal disease in Puerto Rico was limited. Such disease was frequently found due to Shigella paradysenteriae. It appeared that the morbidity and the mortality from this primary enteric infection were well above the rates in the other areas studied. However, there were various other etiologic factors involved, and the relative importance of each was not evident from our data.

We investigated 25 localized outbreaks of diarrheal disease. Sixteen (3 in military camps, 3 in civilian

The literature of the diarrheal diseases is notable for the variability in findings and conclusions. That Shigella infection of some type is the most important single cause has been supported by strong evidence. Flexner and Holt in 1903 were the first to present data leading to this conclusion.[3] They reported on a study of acute diarrheal disease in 421 persons; 273 (66 per cent) had fecal cultures positive for the Shiga or the Flexner variety or both. These results obtained with early bacteriologic procedures at a cost of painstaking and tedious labor were not easily confirmed. In the subsequent study by others of more limited groups of patients, different factors (e. g. parenteral infection)

3. Flexner, Simon, and Holt, L. Emmett: Bacteriological and Clinical Studies of the Diarrheal Diseases of Infancy with Reference to B. Dysenteriae, Rockefeller Institute for Medical Research, 1903.

received attention and emphasis. The observations appear to have served as the basis for generalized opinion. There was an inadequate appreciation of what is now evident. The cause of diarrheal disease varies with area, with season and with age of persons concerned. Statements as to cause must be qualified and limited, not generalized.

EPIDEMIOLOGY

We present here our findings for Shigella paradysenteriae infections and refer only briefly to the epidemiology of other diarrheal diseases.

The rates of incidence are admittedly based on incomplete reports, but in 1937 the rate for culturally proved cases of bacillary dysentery in New Mexico was 2.0 cases per thousand of population, while in 1938, with improved reporting, it was 3.6. South Georgia and Manhattan were studied simultaneously in 1939-1940 and the respective rates for proved cases of bacillary dysentery were 1.7 and 0.04 respectively. It was clear that this infection varied in incidence and occurred more frequently than was usually thought.

symptoms was eleven days, and the average duration of the convalescent carrier state was thirty-four days. The latter terminated by the end of one month in about 50 per cent of the cases but continued for more than ten weeks in 10 per cent. The duration of the passive carrier state appeared to equal approximately the total duration of infection in cases (i. e. the duration of symptoms plus the convalescent carrier state). With rare exceptions all carrier states terminated in less than one year. Chronic carriers, if there are any, are exceedingly rare.

The frequency of occurrence and the distribution by age of the passive carrier state were revealed through culture of fecal specimens from representatives of the general population. A total of 8,643 survey examinations for Shigella was obtained. The persons tested were selected by random sampling. The total discovered prevalence of Shigella infection (i. e. clinical patients, convalescent carriers and passive carriers) was 11 per cent in New Mexico, 4 per cent in Puerto Rico, 3 per cent in Georgia and 0.1 per cent in New York City. A maximum rate of 20 per cent was found

TABLE 3.—*The Prevalence of Shigella Paradysenteriae in Representatives of the General Population as Determined by Survey Fecal Cultures*

Age Group	Number of Survey Cultures	Positive for Shigella Paradysenteriae: Total		Patients with Diarrheal Disease *		Convalescent Carriers *		Passive Carriers *		Others †	
		Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
Under 1 year	416	21	5.0	8	1.9	8	1.9	2	0.5	3	0.7
1 year	193	18	9.3	5	2.6	7	3.6	6	3.1	0	0
2 years	232	19	8.1	4	1.7	8	3.4	7	3.0	0	0
3 years	242	21	8.6	4	1.6	4	1.7	12	4.9	1	0.4
4 years	199	16	8.0	0	0	2	1.0	13	6.5	1	0.5
5-9 years	1,153	94	8.1	6	0.5	13	1.1	73	6.3	2	0.2
10-14 years	781	39	5.0	2	0.3	10	1.3	26	3.3	1	0.1
15-44 years	2,539	115	4.5	6	0.2	26	1.0	78	3.1	5	0.2
Over 45 years	910	32	3.5	1	0.1	10	1.1	18	2.0	3	0.3
Unknown	319	5	0.2	0	0	1	0.3	4	1.3	0	0
Total	6,984 §	380	5.4	36	0.5	89	1.3	239	3.4	16	0.2

* This was the status on the day of examination.
† These include incubatory carriers and person with positive fecal cultures whose status was uncertain.
§ The data on New York City residents (1,659 cultures with 2 positive) are excluded.

There was a definite concentration of culturally proved cases in the younger age groups in New Mexico and Georgia. The annual rate for infants under 2 years reached 30 per thousand in both areas. This rate declined through ages 2 to 4 years. Thereafter the morbidity was low, at the approximate level of 1 case per thousand of population a year. Most of the cases in New York City, in contrast, were distributed rather evenly throughout the first decade, with fewer cases in adolescents and adults.

Among the general population in New Mexico and Georgia the cases occurred chiefly during the summer and early fall. There was a pronounced concentration of cases among the poor. In household groups there were almost as many secondary infections as primary ones. Few young children in infected families remained free of disease. Furthermore, fecal specimens were collected from 219 of the household members who remained well, and 40 (18 per cent) were found to be passive carriers.

Convalescent carriers were identified in considerable numbers. A group of 103 patients whose fecal cultures had been positive were examined by serial cultures following recovery, and 82 (80 per cent) were found to be carriers. The average duration of infection with

in one village. A history concerning diarrhea was taken each time a specimen was secured. Thus we obtained cultural examinations and a record of the number of patients, convalescent carriers and passive carriers at that time. The findings are summarized in table 3. The total of Shigella infections was rather uniformly distributed by age. The highest rates were at ages 1 to 10 years. These were approximately twice those for the first year of life as well as those for the age groups above 10 years. Cases of disease, particularly those of severe disease which normally come to the attention of physicians, were definitely concentrated at younger ages. The passive carrier state was unusual at ages under 1 but increased in frequency with age. More than one half of the children found infected at 3 years and most of the infected older children and adults were passive carriers.

Of the 380 persons whose fecal cultures were positive, only 2 were under the care of a physician. One, acutely ill when found on survey, was admitted to the hospital the following day and died two days later. In the absence of a special study 2 might have been tested culturally, and thus there would have been 2 demonstrated and 378 undetected infections with Shigella. Hence for every known infection (manifest

source) there were numerous unrecognized infections (hidden sources). In the light of these findings it is not surprising that diarrheal diseases commonly appear as sporadic cases. These seemingly unrelated infections may arise from a single source or may be joined by a series of undetected infections. This knowledge is essential for the interpretation of the epidemiology of bacillary dysentery.

The relative frequency of carriers as compared with persons suffering from current diarrheal disease has been observed repeatedly in culturing fecal specimens from groups of institutional inmates. One example follows: An employee in a building which housed almost 200 low grade adult mental defectives had acute diarrhea which proved to be due to an infection with the W variety of the Flexner strain of S. paradysenteriae. No illness had been reported among the inmates, but fecal specimens from all were cultured. On one examination 26 were found to be carriers. This same variety of the Flexner strain was prevalent in inmates of another building who were younger; there were several clinical cases but even here the inmates with current disease were far outnumbered by the convalescent and passive carriers discovered by cultural surveys.

Some information relative to the immunologic response to Shigella infection was obtained through the study of institutional inmates. A preceding clinical infection provided a degree of protection against subsequent clinical attacks with the same variety of Shigella but little protection either against subclinical infection with the same variety or against clinical or subclinical infection with other varieties of Shigella.

Various modes of spread may be effective in the dissemination of these infections; the major question concerns their relative importance. We observed repeatedly a persisting high rate of infection localized in single buildings of institutions which had many buildings served by a common water and a common milk supply and a central kitchen. Flies were either well controlled or were absent because of the season of the year. Neither the water, milk or food nor the flies could be seriously suspected. This negative evidence indicated that the mode of spread was by a direct or an indirect person to person distribution of the infecting organisms.

In Albuquerque, N. M., some sections of the city were free of the disease while in others the infection was prevalent. All used the same water supply. Milk could not be the vector since the poor, who suffered most from dysentery, generally purchased the less expensive sterile canned or dried product. The Indians of the Southwest have a high incidence of diarrheal disease; they also use the sterile canned milk. We saw no evidence which suggested that the etiologic agents responsible for the diarrheal disease were brought into the households in water, milk or any other food product. The disease and the flies were found in the same environment. Still, cultural evidence suggested that flies do not carry Shigella frequently. We obtained only one positive result in repeated attempts to culture Shigella from pooled specimens of flies. In contrast pathogens of this genus were isolated with comparative ease from the fingers or from under the finger nails of culturally positive cases and carriers. On the basis of all evidence we are of the opinion that Shigellas are usually transported through the movements of infected persons (who are more numerous than has been supposed), chiefly those with few or no symptoms. Within the household and within larger groups living together the organisms are passed rather directly from person to person.

With respect to Endamoeba histolytica infection the high prevalence of cyst carriers has been reported repeatedly. However, clinical infection, acute or chronic, is comparatively rare. Both patients and carriers tend to be more numerous in tropical as compared with temperate and colder zones. In our experience apart from the Chicago outbreak cases were observed more frequently in institutions than elsewhere. In contrast to bacillary dysentery infection with E. histolytica was not often observed in infants; most of the subjects were adults.

The ameba carrier state is relatively chronic, its duration being measured in months rather than days and weeks as with bacillary dysentery. The cysts are moderately resistant and may be transmitted from person to person in a viable state through various channels. The wide distribution of E. histolytica is understandable. The unexplained observation is the striking variation in the reaction between host and parasite. In unusual instances the organism assumes the role of a highly invasive and destructive parasite; most commonly it is a seemingly innocuous organism. This striking difference in host-parasite relationship is the outstanding problem in the epidemiology of this condition, and indeed in the epidemiology of many diseases.

The Salmonella infections concerned in diarrheal diseases ordinarily come from animal rather than human sources. The organisms reach man through inadequately cooked meats and eggs, also in food soiled with the droppings of mice and rats. In outbreaks the cases occur within the one to seven day incubation period, though most have their onset on the second and the third day. Secondary cases may occur, but the convalescent carrier state is usually short and in general the infection soon disappears from the involved group.

Parenteral diarrhea is distinctive in its seasonal distribution, which coincides with that of acute infections of the respiratory tract. Outbreaks of staphylococcic food poisoning and "sewage poisoning" are highly explosive and ordinarily begin and terminate within a twenty-four hour period.

CLINICAL FINDINGS

In our studies of the acute diarrheal disorders in general population groups there were included 1,247 cases of diarrheal disease for which clinical as well as epidemiologic and laboratory data were collected. In assembling this series we attempted to secure records of all cases of diarrhea occurring within delimited areas. It is believed that the clinical findings on these cases more nearly represent the true picture of these disorders than the more commonly described observations on hospitalized patients.

One outstanding observation in the study of 555 patients whose stools were culturally positive for one or another variety of Shigella was the wide variation in severity of disease. There was a full range of clinical types from "just a few loose stools" at one extreme to fulminating, rapidly fatal illnesses at the

other. (In addition surveys of the general population revealed large numbers of asymptomatic carriers of Shigella.) Probably of equal importance was the observed fact that the commonest clinical manifestation was a "simple diarrhea." Abdominal pain, anorexia, nausea, vomiting and weakness were reported with frequency in the order named. Fever when present was usually an early manifestation, at times preceding and overshadowing the diarrhea, especially if the invading Shigella was of the Sonne or the Schmitz variety. Additional symptoms less frequently observed were tenesmus, dehydration, loss of weight, convulsions in children and chills in adults. Bloody "dysenteric" stools were seen rather infrequently even in cases of severe disease with positive fecal cultures.

The great majority of diarrheal disorders due to Shigella terminated spontaneously with clinical recovery within a week; those in adults usually in from two to four days. The illnesses in infants were more prolonged, and all 39 fatalities observed were in children under 2 years of age.

Amebic dysentery cannot be differentiated from bacillary infection on clinical grounds alone. In general, clinical amebiasis has a more gradual onset, slower evolution and a greater tendency toward chronicity of symptoms. With acute symptoms the stools are commonly "bloody."

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of endemic acute diarrheal diseases can be made with certainty only in the laboratory by isolation of the specific etiologic agents. Since this involves delay and since the specific chemotherapeutic agents now available for some of these disorders should be given promptly, satisfactory working diagnoses are needed. We suggest below two aids for the establishment of these.

As a first requirement, the most probable diagnosis in the particular area and group must be known. Prior to our studies in New Mexico and Georgia, Shigella infection was thought to be rare and bacillary dysentery was not diagnosed. It was discovered in our work that many of the usual cases of endemic diarrhea, particularly the ones of severe diarrhea, were due to Shigella. From these data the local physicians may know that most of the patients with acute diarrhea who come to their attention have specific enteric infection due to some variety of Shigella. This type of information can be collected through the cooperation of physicians and health departments and should be readily obtainable in military units. Without it the endemic diarrheal disorders will continue to be poorly diagnosed. There must be also an adjustment of the prevailing concept of the clinical nature of "shigellosis"— it must be appreciated that the varieties of Shigella which prevail in this country rarely give rise to the severe bacillary dysentery usually described in medical texts.

Our findings in all areas studied show that Shigella paradysenteriae infection is to be considered as the most probable diagnosis for endemic acute diarrhea occurring in older children and adults, particularly during the warm seasons. This is also true of intestinal disorders of younger children and infants in the South and the Southwest. Other causes, such as parenteral infections and dietary factors, appear to be more commonly involved in early infancy.

A consideration of amebic dysentery is the first step leading to an accurate diagnosis, and this disease is to be considered when persisting, acute, usually "bloody" diarrhea occurs sporadically.

Acute diarrhea caused by Salmonella cannot be differentiated clinically from that due to Shigella. The former tends to give a higher elevation of temperature, more vomiting, greater abdominal tenderness and less blood in the stools. A certain diagnosis must await laboratory findings.

"Food poisoning" due to Staphylococcus is characterized by a brief and stormy course with distressing vomiting, severe diarrhea and little if any fever.

The diagnosis of epidemic diarrheal disease is commonly a joint responsibility of the practitioner and the public health officer. Here the nature of the outbreak provides added information of diagnostic significance. The highly explosive epidemic in which both the outbreak and the cases continue for only a few hours is typical of staphylococcic "food poisoning" and of so-called "sewage poisoning." Infections with true enteric pathogens also occur in explosive outbreaks, but here onsets are distributed through a period of three to seven days, with a peak on the second or the third day. These are most commonly due to some variety of Salmonella, rarely to Shigella. Epidemics due to the latter ordinarily continue throughout a period of several weeks. Characteristically groups previously free from infection at first begin to have sporadic or endemic cases which gradually increase in number. The peak in incidence may be reached only after a month or more. The decline in clinical cases may be more rapid, but the Shigella infection persists thereafter for prolonged periods in convalescent and passive carriers.

LABORATORY DIAGNOSIS

Recent developments in bacteriology have increased the reliability of diagnostic cultural tests for enteric infections. Highly selective mediums which permit growth of the enteric pathogens but inhibit growth of most of the nonpathogens are now available. Fecal specimens obtained by rectal swabs may be used for immediate direct inoculation of the selective mediums. (An ordinary cotton tipped applicator in a small rubber tube having its distal end lubricated is effective and convenient.) For Shigella infections plates of S S agar or desoxycholate citrate agar are used. The surface of the medium is "painted" with the swab. For Salmonella a broth enrichment (selenite F or tetrathionate) is also indicated. Suspected colonies are picked and identified through standard and relatively simple cultural and serologic tests. By using this highly effective procedure, fecal specimens from patients and their contacts may now be cultured in substantial numbers. This examination may and should be employed freely as the most reliable laboratory diagnostic test; it also can be effectively used for the identification of carriers, which is of obvious importance for control purposes.

Microscopic examination of a fresh warm fecal specimen is indicated when amebic dysentery is suspected. Motile amebas with typical characteristics are frequently present in large numbers. Under these conditions a laboratory diagnosis of amebic dysentery may be made with little probability of error. Reliable identification of cysts is more difficult and requires a highly trained worker.

Agglutination tests with the patient's serum cannot be interpreted with sufficient accuracy to warrant the use of this procedure in diagnosing diarrheal diseases.

TREATMENT

Chemotherapy has a place of major importance in the treatment of diarrheal diseases. Emetine and the iodine and arsenic compounds have long been available for amebic dysentery. More recently the sulfonamides have established their place in the therapy of bacillary dysentery and are effective in the treatment of many of the parenteral infections responsible for diarrhea. Specific therapy is not available for Salmonella infections or the "epidemic diarrhea of the newborn." General supportive measures only are needed in "food poisoning" and similar types of diarrhea of short duration.

Two types of sulfonamides are available for bacillary dysentery. There are the poorly absorbed compounds which may be maintained at a high concentration in the intestinal contents while the level in the blood remains low, and there are the more readily absorbed sulfonamides which are also of value in enteric infections. We have studied the clinical and bacteriologic response to three poorly absorbed and five well absorbed compounds. The response to sulfaguanidine, succinylsulfathiazole, sulfadiazine and sulfathiazole has been reported. Since that time we have used these and sulfamethazine, sulfamerazine, sulfapyrazine and sulfathalidine (phthalylsulfathiazole) in more than 1,000 additional persons proved to be infected.

It was evident through a comparison of findings in untreated controls that these sulfonamides all were beneficial in patients with "shigellosis." Flexner varieties of S. paradysenteriae were most sensitive to these preparations and Sonne the least. In general the response to the poorly absorbed sulfonamides tended to be delayed, commonly becoming clearly evident clinically and bacteriologically only after twenty-four hours or more of treatment. There was an earlier response to sulfadiazine and apparently also to the newer well absorbed sulfonamides now under observation. Sulfathiazole has been satisfactory in persons with the Flexner variety of infection but has not evoked as favorable a response as other well absorbed compounds in those infected by the Sonne variety.

Pathogenic types of Shigella presumably do not grow diffusely throughout the contents of the enteric tract, but rather on or in the wall of the bowel. The absorbed sulfonamides are present in the blood stream, and irrespective of route of administration are soon found in high concentrations in the enteric tract. They are rapidly brought by the blood stream to the site of pathologic activity and approach the organisms both from the tissues and from the lumen. The observed response of Shigella infections to absorbed sulfonamides is therefore understandable.

The dose of sulfaguanidine or of succinylsulfathiazole is large, 5 Gm. three times a day for adults being a minimum. During the acute phase of illness, four to six doses may be given daily. We used the well absorbed sulfonamides in 1 Gm. doses three and four times a day in adults. For all preparations the initial dose was twice the maintenance dose. The infections in patients under treatment were followed by daily culture of stools. Medication was discontinued after two consecutive cultures were found negative. On the basis of observations a minimum period of treatment of five days is recommended, to be extended to seven to ten days for infections by the Sonne variety. In all clinical cases treatment should continue for two days following the cessation of symptoms.

Reports in the literature indicate that Shigella dysenteriae (Shiga's bacillus) is inhibited in patients treated with sulfonamide compounds. The data do not indicate the relative sensitivity of this organism to these compounds nor the comparative efficacy of different preparations.

The acute symptoms of amebic dysentery are controlled by emetine hydrochloride, but this drug is a relatively ineffective amebicide. It is a toxic preparation and must be used with caution. The dose for adults is 1 grain (0.065 Gm.) per day, and its use should not be continued longer than the duration of the acute manifestations, with six days as the recommended maximum. For patients with amebic abscess emetine is the only drug of proved value. The available iodine and arsenic preparations are more effective for carriers of the cysts of E. histolytica. The dosages for adults are chiniofon 1 Gm. three times a day for seven days, vioform 0.25 Gm. three times a day for seven days, diodoquin 0.5 to 0.75 Gm. three times a day for eighteen to twenty days and carbarsone 0.25 to 0.5 Gm. twice daily for ten days. All these courses of treatment with iodine and arsenic preparations may be repeated if necessary two weeks after completion. If one proves unsuccessful, another may be tried.

CONTROL

Before sulfonamides became available, control measures were directed to the prevention of direct and indirect spread of human excreta from person to person by means of animate or inanimate vectors. Wherever possible this is still the method of choice since improved sanitation and personal hygiene invariably result in better general health for the individual and the community.

Food poisoning may be prevented by proper care in the handling and preparation of foods. Inadequate cleansing of the hands of the cooks, incomplete cooking of foods and long periods of storage after cooking of custards, puddings and salads are the usual causes of these outbreaks. Insistence on proper care in the kitchen will prevent their occurrence. This is essential also for the prevention of outbreaks due to Salmonella. If cooking is sufficient to raise the temperature throughout all the food being cooked to the thermal death point of these organisms, epidemics of this type will not occur. That they do occur is largely the result of the inadequate recognition of the time required to raise the temperature in the center of a whole fowl, for example, to such a level.

Radical measures are recommended for the control of epidemic diarrhea of the newborn. Nurseries affected are rigidly quarantined. No new admissions are permitted. The sick are separated from the well, and when possible the latter are discharged to their homes. The nursery is permitted to reopen only after thorough sterilization and a vacancy of two weeks.

The problem presented by Shigella infections is more complex. In the general population sanitary measures are a definite aid, but these have not as yet eliminated infections by specific enteric pathogens. In many areas the economic level of the population is such as to preclude effective steps in this direction at present. Adequate treatment of patients with recognized disease will remove some sources of infection, but since patients

with unrecognized infections and persons with subclinical infections are more common, this alone cannot be expected to reduce materially the incidence of endemic disorders. This statement is supported by two attempts to control the spread of Shigella infections (one in a military group and the other in an institution) by administering sulfonamides to all patients irrespective of the severity of their infection as soon as enteric disorders developed. In neither situation were we successful in eradicating or materially reducing the incidence of disease.

In military groups and institutions careful attention to personal hygiene will do much to decrease the incidence of infectious diarrheal disease. When troops have been stationed in permanent well sanitated camps the diarrheal disorders have been a minor problem. Surveys for carriers under these conditions have shown a low prevalence of Shigella infections. The same is true of institutional inmates who are cleanly in their habits and who are housed in a sanitary environment.

However, Shigella infections do gain entrance to groups living under less favorable hygienic conditions. Here they tend to spread widely and remain persistently. In military practice this is most likely to occur among troops in new or temporary camps, during field maneuvers or under battle conditions. Among institutional inmates the mentally disturbed patients and the low grade defectives are particularly involved. A high incidence of carriers is found in association with patients showing bacillary dysentery. Two control procedures have been tested for such heavily infected groups: (*a*) Wherever relatively simple laboratory procedures are available, it is practicable and effective to identify carriers by cultural surveys and to treat all patients and carriers till their stools are culturally negative. The reduction of a high to a very low incidence is readily attained, but complete eradication of all Shigella infections is more difficult. (*b*) The use of small doses of sulfonamides for all persons in such groups also appears promising. A prompt decline in both patients and carriers followed the beginning of this form of preventive therapy in seven groups observed to date. The method must be studied further before it can be recommended as a general control procedure.

In the control of amebic dysentery we urge the necessity of prompt diagnosis and adequate specific therapy to prevent the continuation of the illness and to remove the hazard of death. With regard to the question of treatment of asymptomatic carriers of E. histolytica we believe that widespread effort to detect and treat such persons is impracticable and uneconomical. However, the carrier detected by a physician on routine examination should be treated with one of the iodine or arsenic preparations previously mentioned.

NOMENCLATURE

The term dysentery as ordinarily used implies "bloody stools." The designation bacillary dysentery so interpreted would apply only to unusual cases of Shigella infection. A name referable to the etiologic agent would be preferable. In line with the accepted use of "brucellosis" for all Brucella infections, we recommend the adoption of "shigellosis" for all infections due to pathogenic varieties of Shigella.

National Institute of Health.

PRESENT DAY PROBLEMS OF MALARIA INFECTIONS

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DIAGNOSIS

Malaria infections, either acute or chronic, may be suspected in persons who (*a*) give a history of having had an attack within the previous two or three years, (*b*) who have been residents or transients in an area where these diseases are endemic, (*c*) who exhibit an anemia or splenomegaly otherwise unexplainable, (*d*) who present an acute febrile illness characterized either by a remittent fever or by intermittent febrile paroxysms with or without rigors and unaccompanied by a leukocytosis and (*e*) who present any illness with a comatose onset. Furthermore, unsuspected chronic latent infections may become clinically activated by (*a*) a change in residence involving a material change in climate, (*b*) traumatic injury including surgical treatment and (*c*) confinement. The possibility of a malaria infection must not be overlooked in the recipient of a transfusion who develops fever.

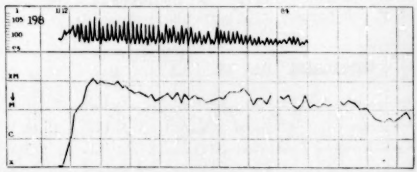

Chart 1.—Naturally induced vivax infection terminating spontaneously. Prepatent period eleven days, incubation twelve days, first clinical reaction with density of 10 parasites per cubic millimeter. Remittent fever from 12th to 14th day, insensibly changing to intermittent quotidian. Spontaneous suppression of paroxysm on the 40th day unexplained. Note gradual decline in temperature from maximum of 107 F. in paroxysm on 19th day to 60th day, when it does not exceed 100 F. Maximum parasite density of about 12,000 per cubic millimeter also on 19th day. Clinical activity ceases spontaneously with concurrent parasite density of about 1,800 per cubic millimeter and is still in excess of 400 per cubic millimeter on 93d day from inoculation.

The charts represent the day by day progress of (*a*) the clinical activity of the infection as reflected in the temperature and (*b*) the parasite density. The first is displayed in the upper portion of the chart and represents the temperature curve in degrees Fahrenheit taken at four hour intervals. The lower portion, on a semilogarithmic scale, represents by a solid line the density of total parasites (trophozoites and gametocytes) per cubic millimeter as determined from smears routinely taken at about 8 a. m. If the gametocyte density is shown, it is represented by a line of dots and dashes. The lowest line of the 1st cycle of ruling represents a density of 10 parasites per cubic millimeter, the second 100, the third 1,000, the fourth 10,000 and the fifth 100,000. The vertical lines mark the days elapsing since the inoculation by means of infected mosquitoes, the day of which is further marked by the arrow.

By the terms of our definition a definitive diagnosis must be based on the detection of the parasites in a blood smear. Other tests, largely of a serologic nature, have been proposed, some of which may have merit. From the standpoint of convenience and speed these are not, in my opinion, likely to supplant the examination of blood smears. In consideration of laboratory reports, it should be borne in mind that a single or even several negative examinations are insufficient to exclude

From the Station for Malaria Research.

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Owing to lack of space, this paper has been abbreviated for publication in THE JOURNAL. The complete paper appears in the author's reprints.

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the existence of a malaria infection. On the other hand, the detection of a single parasite of unimpeachable morphology is sufficient to recognize the existence of such an infection but would not necessarily justify the attribution of the patient's symptoms to their presence.

Blood smears for malaria diagnosis should be taken with the utmost care and should afford a thin and thick smear on the same slide. The limitations of space do not permit a discussion of the technics for making and staining smears and the morphologic identification of parasites. These are given by Wilcox.[5] The recent ingestion of antimalarial drugs by a person with a latent infection may make parasites undetectable for some days thereafter. The examination of a thick smear for five minutes is roughly equivalent to the examination of a thin smear for fifteen minutes, thus effecting material saving of time in a busy laboratory. If parasites are not detected within this time it is hardly worth while to spend further time in the examination of this smear, as it is preferable to collect further smears on the following days. However, delays in diagnosis incidental to low parasite densities will not adversely affect later therapy. The report should if possible also specify the identification of the species of any parasite observed. In the event of a diagnosis of P. falciparum, it is particularly desirable to determine the density of parasites per cubic millimeter, for it must be remembered that the clinical attack is but a reflection of the course of the parasitemia. For this the method of Earle and Perez[6] is useful. It is also desirable to control the effectiveness of the treatment of acute malaria by the daily examination of blood smears continued until the smears become negative.

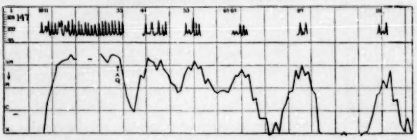

Chart 2.—Naturally induced vivax infection, with an induced remission followed by a series of recrudescences and a relapse. The incubation period was of ten days, the prepatent period eleven days. Attack an intermittent quotidian from onset. However, on 15th and 16th and again on 17th and 18th the febrile periods were of about thirty-six hours' duration, with bifid peaks. While common in falciparum infections, these protracted paroxysms are unusual in vivax malaria. A single 10 grain (0.65 Gm.) dose of quinine sulfate given on the 33d did not affect the paroxysm on that or the following days. It did result in a definite depression of the parasitemia, which reached a minimum on the 38th day. Coincident with this depression, a remission occurred which lasted from the 35th to the 40th day. Although the density of the parasitemia was again as high on the 42d day as it was when the quinine was given, it did not remain sustained but underwent a succession of four further depressions and rises, with a clinical remission occurring at each depression and a renewal of clinical activity during each rise. The first four rises are recrudescences, the fifth is a relapse. Note that each period of renewed clinical activity is initiated by tertian paroxysms.

The lowest parasite density which may be recognized by examination of a smear for the time suggested is approximately 10 parasites per cubic millimeter. In highly susceptible persons clinical activity may, as already noted, be initiated by lower and submicroscopic densities. On the other hand, at the onset of relapses the parasite density will be high, often several thousand per cubic millimeter, as might be expected in a partially immune person (charts 2 and 3). Quartan and vivax infections commonly exhibit a ceiling to the maximum parasite densities attained. The quartan parasitemias seldom exceed 10,000 per cubic millimeter (chart 8) and those of vivax seldom exceed 50,000 per cubic millimeter (charts 1, 2, 3 and 4). On the other hand, the falciparum parasitemia has no potential limits (charts 5, 6 and 7) and it is important to note that the prognosis is definitely bad if the count attains or exceeds 500,000 per cubic millimeter. The employment of provocatives in suspected latent infections, either to expel parasites from the spleen or to induce a relapse, have not, in the hands of my associates and myself, given sufficiently consistent results to warrant their routine utilization as aids to diagnosis.

It is a matter of regret that many physicians practicing in endemic areas, have based diagnoses of malaria infections on clinical histories, as some still do, and often on the relation by a patient of obscure and, for malaria, atypical complaints. While recognizing that an experienced practitioner will often, perhaps usually, correctly recognize typical intermittent attacks from their clinical manifestations alone, I am of the opinion that this is nevertheless an unfortunate and undesirable practice. It has undoubtedly resulted in ascribing to malaria many conditions for which these infections are not to blame[7] and has probably contributed in no little degree to the extent to which real or imaginary sufferers indulge in self medication. The burden of proof lies on the diagnostician.

SALIENT CLINICAL FEATURES

Although malaria is a self limited disease, comparatively few physicians in the centuries which have passed since the introduction of cinchona have had opportunity to observe the uninterrupted evolution of these infections, as in general they felt in duty bound promptly to administer the bark, or later the alkaloids, and hence abruptly to interrupt the attack. Therefore the application of induced malaria to the therapy of neurosyphilis, particularly when naturally induced, affords a unique opportunity to reappraise and verify ancient knowledge and extend observations of the experimental disease along modern lines of investigation.

Clinically active malaria infections regardless of the species of their causative parasite exhibit three basic symptoms: (*a*) fever, (*b*) anemia and (*c*) splenomegaly. The first two are definitely related to the development of the parasites, as the fever occurs at the time of their multiplication, and the anemia arises from the destruction of the erythrocytes on which the parasites have fed. The specific infections, particularly falciparum malaria, may in addition exhibit other and very striking symptoms. To one who wishes to pursue this subject further the classic monographs of Marchiafava and Bignami[8] and Mannaberg[9] still offer the best extended clinical descriptions.

Fever is the most striking manifestation of clinical activity and may at times be remittent but is more commonly intermittent. Vivax infections in susceptible persons frequently present a remittent fever for a period of from three to five days at the onset (chart 1). Falciparum infections likewise often exhibit a remittence (chart 7). Although such sustained temperatures

5. Wilcox, A.: Manual for the Microscopical Diagnosis of Malaria in Man, Bulletin 180, National Institute of Health, Federal Security Agency, United States Public Health Service, 1942.

6. Earle, W. C., and Perez, M.: Enumeration of Parasites in the Blood of Malarial Patients, J. Lab. & Clin. Med. **17**: 1124-1133, 1932.

7. Fondé, G. H., and Fondé, E. C.: Chronic Malaria: Clinical Consideration, Arch. Int. Med. **64**: 1156-1169 (Dec.) 1939.

8. Marchiafava, E., and Bignami, A.: Malaria, in Stedman, T. L.: Twentieth Century Practice, New York, W. Wood & Co., 1901, vol. 18.

9. Mannaberg, J.: Malarial Diseases, in Nothnagel, C. W. H.: Encyclopedia of Practical Medicine, edited by A. Stengel, Philadelphia, W. B. Saunders Company, 1905.

are clearly due to lack of synchronization in the sporulation time of the parasites, pronounced secondary rises or peaks are usually noted, which indicate the sporulation of large groups of parasites and forecast the later intermittence. The transition from remittence to intermittence is thus usually gradual. The intermittent paroxysms may recur every day (quotidian, chart 1), every other day (tertian, charts 2, 3, 4, 6 and 7) or every fourth day (quartan, chart 8). In the intervals between paroxysms the temperature oscillates within normal limits. About ten days after the onset of the primary attack in susceptible persons, or at the onset of a relapse, the paroxysm is often initiated by a rigor or chill, which may vary in intensity from a slight subjective sensation of chilliness to involuntary muscular contraction accompanied by a sensation of extreme cold. The temperature is meanwhile rapidly rising, but before the peak of the fever is reached the patient is no longer cognizant of cold. At the maximum of elevation, which is not long sustained, profuse perspiration sets in, and the temperature rapidly falls as in a crisis. With the return of normal temperature the patient may become ambulatory and except for a sensation of weakness the vivax infected patient may offer no complaint. However, the quartan paroxysms are definitely more exhausting and the protracted falciparum paroxysms still more so. The period during which the temperature remains elevated during a paroxysm varies with the different infections, in vivax for from six to twelve hours, in quartan from eight to twelve hours and in falciparum malaria from six to thirty-six hours. The vivax and quartan paroxysms usually exhibit a rapid and symmetrical rise and fall of temperature to and from the peak. The protracted falciparum paroxysms may have a sustained period of elevation or have bifid or trifid secondary temperature peaks (chart 7). The regularity and uniformity in the successive paroxysms in vivax and quartan malaria is in sharp contrast to the irregular and asymmetrical fever curve of the paroxysms of falciparum malaria. The maximum temperature attained in a vivax or quartan paroxysm varies to some extent with the current density of the parasitemia and may briefly attain as high as 107 F. or more with no immediate risk to the patient or forecast of a dangerous trend in the infection. On the other hand, an observation of 104 F. or higher in falciparum malaria, particularly if the course is remittent, suggests that the infection may soon get out of hand. It should be stressed that primary vivax infections usually exhibit a series of quotidian paroxysms and that tertian paroxysms are not usually seen until the attack is wearing out or during relapses (charts 2 and 3). Quartan infections usually present paroxysms recurring every fourth day (chart 8) but, as the infection evolves, a new cycle may be injected and the patient will exhibit paroxysms on two consecutive days followed by one paroxysm free day and finally, with the appearance of a third cycle, develop quotidian paroxysms. Thus quotidian paroxysms in vivax malaria are due to the division of two alternating broods of parasites, each requiring forty-eight hours for maturation, and in quartan malaria to the division of three consecutively maturing and overlapping broods, each requiring seventy-two hours. As the infection progresses, synchronization of the parasites improves and the duration of the paroxysm diminishes, while a diminution in the maximum elevation of the temperature forecasts early extinction of clinical activity by the corresponding brood of parasites (chart 1). The alternating parasite broods which produce vivax quotidians are not indicative of inoculation on two successive days (charts 1, 2 and 3). While the paroxysms due to any brood in vivax and quartan infections tend to recur at the same hours, more frequently afternoon than forenoon, some broods for reasons not understood take less or more than the conventional forty-eight or seventy-two hours and hence the paroxysm cycles recur earlier (anticipation) or later (postponement) and may finally run around the clock.

Some patients with grave falciparum infections will not subjectively complain of fever but exhibit a cold skin and clammy perspiration, with cyanosis of the extremities. This often accompanies manifestations of gastrointestinal symptoms. It may occur at the onset or after several more or less typical paroxysms.

The development of the anemia may be gradual or rapid and is accompanied by a pallor to which vasomotor disturbance might contribute. It develops most slowly and to the least degree in quartan infections, probably because of the slower growth and lesser density of these parasites, as well as from their predilection for the aging erythrocytes. It progresses more rapidly

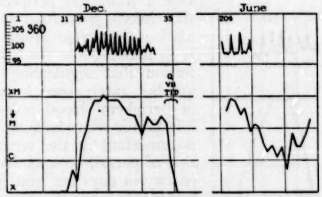

Chart 3.—Naturally induced vivax infection, with spontaneous remission during which divided doses of quinine were given during three days, patient later experiencing a recurrence. Note prepatent period of eleven days, incubation period of fourteen days. Slight remittence for three days after onset, followed by protracted paroxysms on 17th-18th and 19th-20th, with bifid peaks, thereafter proceeding as a quotidian. Termination of attack spontaneous on 30th with about 1,500 parasites per cubic millimeter. During the remission 7 grains (0.45 Gm.) of quinine was given twice daily for three days, which drove the parasitemia to submicroscopic levels. On the 204th day following the inoculation the patient had the first renewal of clinical activity, which initiated the first of a series of four tertian paroxysms. The day following the first paroxysm of the recurrence, a parasitemia of about 3,500 per cubic millimeter was observed.

in vivax infections and is probably intensified by the predilection of these parasites for the reticulocytes. Most rapid progress, however, is seen in falciparum infections, which is attributable not only to the greater parasite density attained but by their attack on erythrocytes of all ages. The anemia is hypochromic in type. Since the iron stores are not depleted by this destruction of cells, progress toward restoration of blood loss is rapid during remissions. It is interesting to note that spontaneous remissions usually occur in vivax infections when the erythrocytes are reduced to about 1.5 million per cubic millimeter with hemoglobin about 4.0 Gm.

Enlargement of the spleen is detectable during the second week following the primary onset. The splenic border is rounded, the organ is obviously tense and palpation may be painful. In one attack the enlargement may bring the lower pole to the vicinity of the umbilicus in the course of two or three weeks. With cessation of clinical activity the congestion may rapidly subside or some degree of enlargement may persist indefinitely. Such persisting enlargement suggests

that a latent infection continues.[10] The contracting spleen appears flaccid to the palpating fingers and is found lying more toward the left flank. With repeated enlargement due to either relapses or reinfections the organ may extend to the pelvis, fibrosis develops, probably stimulated by the pigment deposits, the substance becomes firm, the border is sharp, and involution proceeds slowly. The liver may also be enlarged and tender.

Albumin is frequently noted in the urine in amounts exceeding a trace, in infections produced by any species of parasites. However, this is most variable in vivax infections and most consistently noted in quartan infections. In falciparum and quartan this is usually associated with a depression of the plasma albumin. During the period of this depression there may be rises in the globulin and euglobulin values. Edema of the extremities is least commonly observed in vivax infections and is most frequent with quartan. In the latter its occurrence may be anticipated with depression of the plasma albumin. The conjunction of edema, albuminuria and reduction in plasma protein leads to the conclusion that a malaria infection produces a nephrosis rather than a nephritis.[11]

In vivax, but more particularly in falciparum infections, the maturing parasites exhibit a tendency to recede from the peripheral to the visceral circulation as sporulation time approaches. This is so noticeable in the latter infection that segmenting forms are but rarely seen in smears of peripheral blood unless the infection is overwhelming. This is important in the interpretation of parasite counts made on paroxysm days but prior to the paroxysms, as these will be much lower than those observed in the interpyrexial days (charts 5, 6 and 7). In this retreat the parasites, for reasons unknown, appear more particularly to congregate in the capillaries of some particular viscus of the cerebrum, lungs or intestine. Since the erythrocytes infected with these parasites appear shrunken and rigid and, owing to a coating of fibrin appear adhesive,[12] they produce extensive capillary blockade. Consequently falciparum infections more particularly may present additional striking and variable symptoms, which are often referable to the viscus in which sporulation is occurring and which may mislead the physician unless blood smears are routinely taken. Space does not permit detailed discussion of these nearly infinite variations, which have received elaborate clinical classifications,[13] but special mention may be made of (*a*) continued fever with or without hyperpyrexia, (*b*) hypopyrexia, (*c*) various cerebral manifestations including coma, delirium and convulsions, (*d*) various symptoms referable to the gastrointestinal tract including persistent vomiting, often bilious, dysenteric or diarrheal evacuations, sometimes with hemorrhage from the bowel, (*e*) symptoms suggesting acute bronchitis or pneumonia, (*f*) weak pulse and syncope, thrombosis and hemorrhages, edema and dropsy, acute progressive anemia, sometimes hemolytic, (*g*) icterus, (*h*) albuminuria, hematuria and hemoglobinuria. The latter condition is often differentiated as blackwater fever.

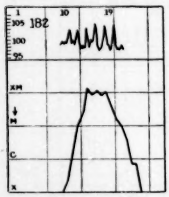

Chart 4.—Naturally induced vivax malaria with early spontaneous termination. Prepatent period ends on 10th day and incubation ends on 11th day, initiating a series of tertian paroxysms which cease spontaneously on the 21st day. Note the rapid spontaneous decline in the parasitemia beginning on the 20th day and descending to submicroscopic levels on the 27th day. This patient must have had previous experience with some other strain of vivax parasites, as he exhibits a heterologous immunity.

Untreated primary attacks may vary greatly in their duration, depending on the degree of the patient's susceptibility and the species of parasite. Quartan infections may continue clinically active for as long as nine months (chart 8), vivax infections, spaced out by spontaneous remissions, may continue for approximately one hundred days (chart 2), although if remissions do not intervene I have not observed them to exceed nine weeks (chart 1), while falciparum infections are the shortest and will not often exceed six weeks in duration (charts 6 and 7). In these protracted infections the severity of the paroxysms gradually diminishes coincident with a reduction in the elevation of the temperature. The change may be more pronounced in one cycle than the other, in which case the cycle most affected may drop out and the course is continued as a tertian. The termination of the course is similar to a lysis (chart 1). In my opinion any clinical activity noted within these limits, even though interrupted by one or more spontaneous remissions, is essentially attributable to the primary parasitemia. In such patients clinical activity ceases while the parasite density is still high (chart 1), and the latter gradually decreases but persists at microscopic levels for several weeks.

In falciparum infections gametocytes are not observed until about ten days after the first appearance of trophozoites (charts 5, 6 and 7). Their appearance is frequently made manifest by a sharp decline in the density of trophozoites often sufficient to produce a clinical remission. This may mark the end of the attack (chart 5). In more susceptible persons trophozoites will return to pyrogenic levels in about ten days more, and clinical activity will be resumed (chart 6). A falciparum attack will consist of one or more such units of alternating waves of trophozoites and gametocytes (charts 6 and 7). In vivax infections gametocytes are present practically from the onset, while in quartan their production is scanty and irregular. Since both clinical activity and gametocyte production are proportional to the density of the parasitemia, those who are, or who have recently been, clinically ill will be the most infectious to anophelines, both qualitatively and quantitatively. After latency is well established, patients may again become slightly infectious if subclinical rises occur in their parasitemia.

However, vivax and quartan infections whose natural evolution has been interrupted by early remissions therapeutically induced show a definite and annoying tendency to resume clinical activity at a later date, even after the lapse of a year or more (chart 3). Falciparum infections probably do not persist in a latent condition for more than a year, vivax may persist for two or perhaps even three years, while quartan latency may persist for protracted and unpredictable periods. Resumption of clinical activity, if occurring within eight weeks of the cessation of the primary attack, is dis-

10. Stratman-Thomas, W. K.: Studies on Benign Tertian Malaria: Observations on Splenomegaly, Am. J. Hyg. **21**: 361-363, 1935.

11. Boyd, M. F., and Proske, H. O.: Observations on the Blood Proteins During Malaria Infections, Am. J. Trop. Med. **21**: 245-260, 1941.

12. Knisely, M. H.; Stratman-Thomas, W. K., and Eliot, T. S.: Observations on Circulating Blood in the Small Vessels of Internal Organs in Living Macacus Rhesus Infected with Malarial Parasites, Anat. Rec. (supp. 2) **79**: 90, 1941.

13. Marchiafava and Bignami.[5] Mannaberg.[9]

tinguished as a recrudescence (chart 2) and, since practically all these arise within one hundred days of the onset, before the primary parasitemia has descended to submicroscopic levels, should properly be regarded as part of the primary attack. Further clinical activity occurring in from eight to twenty-four weeks after the cessation of the primary attack is designated a relapse, and if arising after an interval longer than twenty-four weeks it is known as a recurrence (chart 3).

Persons who have had previous experience with other strains of the same species of parasite will experience attacks of varying duration but usually of not over two weeks (chart 4). These terminate abruptly with a rapid decline in the parasitemia.

TREATMENT

The treatment of malaria infections is symptomatic and specific. The former is practiced concurrently with the specific, chiefly to alleviate symptoms which distress the patient or interfere with specific treatment; specific therapy is directed to the destruction of the parasites.

Until the fever is checked the patient should be confined to bed, while for two weeks subsequently activity should be limited to very moderate ambulatory exercise.

If the hyperpyrexia observed during a paroxysm is due to sporulation of parasites alone, its duration will be transitory and will rarely require interference except for the comfort of the patient. If it persists it may be suspected that the cerebral heat centers are affected. In this case tepid sponging or cold baths may be employed, their duration being controlled by the rectal temperature. During this time an abundant intake of cool fluids should be encouraged, which should be supplemented by sodium chloride. When free perspiration is begun the patient should be rubbed dry and changed to dry clothing. On the other hand, if the temperature is subnormal the patient should be well provided with covers and numerous hot water bottles. Several sinapisms should be applied to different parts of the body, and hot beverages should be supplied. Since these patients often suffer from constipation, purgation should be effected if necessary, and daily doses of liquid petrolatum given subsequently. Nausea, and vomiting in particular, may interfere with the oral administration of specific drugs. They may often be controlled by cracked ice with or without lime water. If uncontrollable by this means, 5 minims (0.3 cc.) of tincture of opium or 5 to 20 grains (0.3 to 1.3 Gm.) of chlorobutanol may be given. Other symptoms are appropriately met as the need arises. Patients with edema should receive a high protein diet, and those with icterus a high carbohydrate and vitamin diet.

An excellent discussion of the treatment of malaria, based on an extensive experience, has been presented by Dove,[14] while the monograph of Field [15] is the most exhaustive recent treatise. The Fourth General Report of the Malaria Commission of the League of Nations should also be consulted.[16]

The specific treatment of malaria is parasiticidal and must take into consideration the different stages of the parasites which are concerned with the human host, namely the infecting or sporozoite stage, the vegetative (trophozoite) stage, to the multiplication of which clinical activity is due, and the gametocytes which render the patient infectious.

Of recent years the specific therapy of malaria has undergone profound modification, owing (1) to an enlargement of the physician's armamentarium by the introduction of the useful synthetics plasmochin and atabrine, (2) to the recent capture of the principal areas of cinchona production by the enemy, which have caused available stocks of the alkaloid quinine to be reserved for military use and the substitution therefor of totaquin, a standardized preparation containing all of the crystallizable alkaloids present in American barks, and (3) the possibility that current research may result in the discovery of still more efficient synthetics. Information of progress in this field of research will likely be withheld until the end of the war. Present dosage regimens of antimalarial drugs have largely developed empirically. It is hoped that present studies on attainable concentrations in the blood will permit of their more scientific utilization.

SUPPRESSIVE TREATMENT

Quinine has been routinely taken for years by those resident in endemic areas, and of later years atabrine has been similarly ingested, in the belief that it will

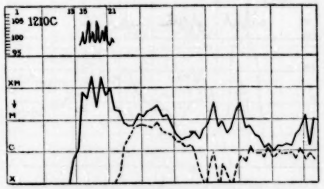

Chart 5.—Naturally induced falciparum malaria in a Negro patient, the attack terminating spontaneously. Prepatent period ends on 13th day, incubation period on the 15th day. Attack consists of a series of six unequal quotidian paroxysms. The cycle of the day of onset, on that and the subsequent days of its tertian reappearance, is distinctly weaker than its alternate. The maximum parasite density attained was about 24,000 per cubic millimeter, a low density for this parasite. Clinical activity ceased spontaneously because of a coincidental drop in the parasitemia density on the 22d, on which day gametocytes were first seen. The trophozoite minimum was reached on the 26th, they increased slightly for five days thereafter, and then they underwent a second decline and a further rise, neither of which was accompanied by clinical activity.

ward off infection from the bite of an infected mosquito. Any drug that might possess the property of destroying sporozoites or the succeeding stage of the parasites would be a true causal prophylactic. Unfortunately quinine does not possess this property, nor is it dependably exerted by atabrine, nor is there any other known available drug which possesses this characteristic. This deficiency in these drugs, or misconception of their properties, should not however deter us from their employment under certain circumstances. While they will not prevent a person from contracting infection, they will check the multiplication of parasites sufficiently so that most protected persons will not develop active clinical malaria during the period in which they are ingested. Their employment is thus more appropriately described as suppressive treatment. Their routine distribution where large bodies of men are suddenly brought in an emergency into unsanitated areas for construction or military purposes will temporarily avoid the incapacitation of many from malaria. However, on the withdrawal of these men from such areas and with the suspension of treatment many will develop

14. Dove, W. S.: The Treatment of Malaria, Am. J. Trop. Med. **22**: 227-234, 1942.
15. Field, J. W.: Notes on the Chemotherapy of Malaria, Bulletin 2 of 1938, Institute for Medical Research, Federated Malay States, Kuala Lumpur, 1939.
16. The Treatment of Malaria: Study of Synthetic Drugs, as Compared with Quinine, in the Therapeutics and Prophylaxis of Malaria, fourth general report of the Malaria Commission, Quart. Bull. Health Organ., League of Nations **6**: 895-1153, 1937; off-print no. 5, Geneva, 1937.

acute clinical malaria about two weeks later. As at present practiced, adult males are given 0.1 Gm. of atabrine daily at the evening meal on six days each week. The practice is not an adequate substitute for sanitation.

TREATMENT OF THE ACUTE ATTACK

The attack on the schizogonous cycle of the parasites constitutes the specific therapy of the active infection, and for this purpose the civilian practitioner is now practically limited to totaquin and atabrine dihydrochloride. From the standpoint of their parasiticidal action the properties of the two drugs are closely parallel, and there is little choice between them, but effective concentrations in the plasma are built up more rapidly in the case of the cinchona alkaloids. The assault on the schizogonous cycle should be directed to two objectives. The first is the treatment of the acute attack, by which it is sought to reduce the parasitemia to such low levels that a clinical remission results. An acute attack may be the manifestation of a primary infection, a recrudescence, a relapse or a recurrence. This is usually readily accomplished. The second should be the eradication of the infection from the human host or the accomplishment of a cure. This requires treatment of the latent infection. With available drugs this result is highly uncertain, and under

Chart 6.—Naturally induced falciparum infection in a white patient. Prepatent period ended on 9th day, incubation period ended on 10th day. Density of parasitemia exceeded 100,000 parasites per cubic millimeter on the 14th day, necessitating administration of single 0.6, 0.3 and 0.6 Gm. doses of quinine on the 14th, 15th and 16th days to control its exuberance. It is not apparent that these contributed to the drop in parasite density on the 18th day, coincidentally with the appearance of gametocytes. It should be noted that each period of clinical activity is attributable to a wavelike rise in the trophozoite parasitemia and that the density of trophozoites fell off with the appearance of gametocytes, each resulting in a spontaneous remission in the attack. During the period of observation, each of the first three trophozoite waves has been followed by a wave of gametocytes, which reached their maximum during the remissions.

ordinary circumstances success is not readily demonstrable.

Certain general principles should be observed in the employment of plasmodicidal drugs. Oral administration is always the route of choice, and the occasions when parenteral administration is required are unusual. Absorption from the stomach is so rapid that no material time is saved by parenteral administration. Parenteral administration should be limited to comatose patients or those with hyperpyrexia or in whom vomiting has proved uncontrollable. If parenteral administration is required, atabrine rather than quinine should be the choice, and the intramuscular rather than the intravenous route should be selected. It should, however, be mentioned that quinine dihydrochloride is still available for parenteral therapy. Injection should be made deeply into the gluteal muscles of both buttocks at a point about 3 inches below the iliac crest, with subsequent thorough massage of the site. Such an injection may be repeated after twelve hours but should not be continued after the patient can take medication by mouth.

The dosage of the drug employed must be adequate and should be initiated as soon as practicable after diagnosis is effected. Certain strains of P. falciparum appear to require larger doses to effect a satisfactory response, but I am skeptical that a parasite strain is likely to acquire a drugfastness. Differences in the strains of parasites prevalent in various regions probably account for divergences in reaction to treatment. While in general totaquin, like quinine, should be administered before meals and atabrine after meals, one of the daily doses should be scheduled to be given about one hour before the occurrence of the next anticipated paroxysm in order that a maximum plasma concentration may be available when the young merozoites are liberated. It should not be expected that the initiation of treatment will forestall the next anticipated paroxysm, or even the one due on the following day, but if treatment is adequate and the drug is properly absorbed, paroxysms should not occur on the third and subsequent days. It is helpful to control the effect of the drug by daily parasite counts. If quinine has been employed, only exceptional patients will show a few parasites, other than falciparum gametocytes in smears taken on the fifth day after treatment was initiated. If atabrine was administered, a few patients may exhibit parasites as late as the seventh day. During these periods the counts on successive days should exhibit a progressive decline. If these conditions are not soon met, it should be ascertained whether the patient is absorbing and excreting the drug, by applying appropriate tests to the urine. While not incompatible, nothing is gained by undertaking to administer the two drugs concurrently.

Totaquin (totaquina) is a preparation originally developed under sponsorship of the Malaria Commission of the League of Nations in order to supply a cheaper effective antimalarial drug through the utilization of all the alkaloids from cinchoma barks the quinine content of which is too low for the profitable extraction of that alkaloid alone.[17] Under present circumstances this is the most efficient manner in which to employ the limited stocks of American barks, which are the only supply available, and utilize the parasiticidal properties of the other crystallizable alkaloids of cinchona which have heretofore been largely ignored, although they are just about as effective plasmodicides as is quinine.[18] The preparation as standardized in accordance with the U. S. P. XII contains not less than 7 nor more than 12 per cent of anhydrous quinine, and a total of not less than 70 nor more than 80 per cent of the anhydrous crystallizable cinchona alkaloids, the latter term including quinine, quinidine, cinchonine and cinchonidine.[19] It should be prepared in friable tablets or placed in capsules for administration by mouth and should be administered in doses corresponding to those of quinine sulfate. It should not be given in fluid mixture. Totaquin is not available for parenteral administration. It is probably as inadvisable to administer totaquin to a pregnant woman as it would be to administer quinine. Totaquin should be administered to adults in divided doses in not less than 0.6 Gm. (10 grains) daily per 50 pounds (23 Kg.) of body weight.

17. The Therapeutic Efficacy of Totaquina in Human Malaria, Quart. Bull. Health Organ., League of Nations **3**: 325-358, 1934.
18. Dawson, W. T.: Cinchona Alkaloids and Bark in Malaria, Internat. Clin. **2**: 121-149, 1930. Fletcher, W.: Notes on the Treatment of Malaria with the Alkaloids of Cinchona, London, John Bale, Sons & Danielsson, Ltd., 1923.
19. Weed, L. H.: Critical Antimalarial Problem and Its Solution, J. A. M. A. **120**: 1043-1044 (Nov. 28) 1942.

For an adult of 150 pounds (68 Kg.) this is the equivalent of 0.6 Gm. or 10 grains three times a day. Adult dosage may be given to all over 12 years of age. Dosage for children should be reduced in proportion to their age, while a baby may be given at least 0.06 to 0.09 Gm. (1 to 1½ grains). Field [20] considers that children should be given proportionately large doses. Doses should be given before meals and continued for seven days.

Prior to the last decade it was commonly recommended that a daily ingestion of 0.6 Gm. of quinine be continued for eight weeks after the acute attack was brought under control, in the belief that relapses were largely avoided thereby. It is doubtful whether many patients can be depended on to continue such protracted medication, while the convenience of the short period required for a single course of atabrine has tended to stimulate a curtailment in the period over which quinine is now frequently administered. The concurrent administration of plasmochin 0.01 Gm. thrice daily after meals is, however, considered a desirable adjuvant in the treatment of vivax infections, as lessening the likelihood of a relapse. Absorption of some of the cinchona alkaloids at least is rapid, excretion of quinine being detectable within fifteen to twenty minutes after the administration of a dose. Excretion is detected by the application of Tanret's test to the urine.[21] While tinnitus and deafness may be an inconvenience to the patient, they are reassuring evidence of absorption. If the other cinchona alkaloids behave similarly to quinine, it may be assumed that the greater quantity is disintegrated in the body and that such slight stores as have accumulated are fully depleted within seventy-two hours after the last dose of a course is taken.

Atabrine dihydrochloride, or quinacrine, is an acridine dye developed in 1930 by Kikuth with the collaboration of Mietsch and Mauss. It is available in 0.1 Gm. tablets. Prior to our entrance into the war the complete synthesis of atabrine in the United States was not practiced. In view of the critical quinine situation it is fortunate that American chemists have succeeded in its synthesis and that large scale manufacture is now under way. Extensive chemical, pharmacologic and clinical studies have demonstrated that the American product is in all respects identical with the German drug.[22] It has now been admitted to the United States Pharmacopeia under the name "quinacrine."

While most persons tolerate the doses recommended, a few may not support without discomfort even the mild regimen of suppressive treatment. These complain of headache, dizziness, nausea and vomiting, and diarrhea. These reactions are avoided by the concurrent administration of alkaline or sweetened beverages. Less frequently the drug has been reported to have produced a definite slowing of the respiration and cerebral excitation which may even attain maniacal proportions.

Atabrine is usually administered to adults after meals, one 0.1 Gm. (1½ grain) tablet being given three times (four times to large adults) a day for five days, or at least until four days have elapsed since the last fever. Children under 1 year may tolerate a total daily dose of 0.05 Gm., from 1 to 4 years of age 0.1 Gm., from 5 to 8 years 0.2 Gm., and those over 8 may be given a daily total of 0.3 Gm.[23] These fractional doses are best given in milk.

In order to accelerate the action of atabrine by more quickly building up an effective plasma concentration, it is now recommended that adults initially receive 0.2 Gm. (3 grains) by mouth every six hours for five doses, which is thereafter reduced to 0.1 Gm. (1½ grains) three times a day for six days. The early elevated doses are accompanied by 1 Gm. (15 grains) of sodium carbonate in 200 to 300 cc. of water, sweetened tea or fruit juice.

For parenteral administration a dose of 0.2 Gm. may be dissolved in from 5 to 10 cc. of sterile distilled water. The effect of atabrine is not exerted as rapidly as that of quinine, a difference attributable to notably slower absorption, although urinary excretion is detectable within a few hours. Neither is its excretion as rapid, and the drug tends to accumulate, so that excretion continues for five weeks or more after the termination of a course. This may be the chief advantage of atabrine over quinine. Its excretion in the urine may be verified by the method of Wats and Ghosh.[24] For this reason courses of atabrine should not be repeated in less than a month's time. The small margin of safety between the therapeutic and toxic doses is probably related to the rapidity with which the blood level is raised and makes

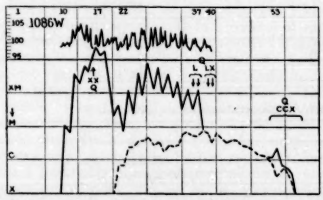

Chart 7.—Naturally induced falciparum infection in a white patient. Prepatent period ended on 10th day, incubation period on 12th day by a period of remittent fever lasting five days and changing to an irregular intermittent, which later became tertian, exhibiting prolonged paroxysms with bifid peaks suggestive of a quotidian. On the 17th day the parasitemia density exceeded 200,000 per cubic millimeter, when two 0.6 Gm. doses of quinine were given. This effectively restrained the exuberance of the parasitemia. The parasitemia was declining the day before gametocytes were first noted, but the decline was insufficient to produce a clinical remission, although the coincidental paroxysms were notably weaker. With the return of the trophozoites the counts on successive days oscillate widely. The attack was terminated by a total of 3.3 Gm. of quinine on the 37th and 38th day and a total of 4.0 Gm. on the 40th and 41st. Note the resistance of the gametocytes to these doses. Evidently the gametocyte waves which corresponded to the two trophozoite waves have fused. On the 53d day there began a seven day course of quinine, during which 14 Gm. of quinine was given.

it essential to avoid overdosage and the development of accumulations which may reach toxic levels. As the drug accumulates the patient may exhibit a yellowish discoloration of the skin, which should not be mistaken for jaundice but is a manifestation of its dye property. Plasmochin should never be concurrently administered, as gastric complications, pain and loss of appetite may occur.

Although intravenous therapy is counseled against, occasions may arise when it is considered imperative. It should not be continued after medication can be taken by mouth. The dose should be well diluted in at least 200 cc. of sterile saline solution and at least twenty minutes allowed for the injection. In the case of quinine particular care should be taken to see

20. Field, J. W.: Notes on Totaquina, League of Nations Health Organization, Official No. C. H. Malaria/214, Geneva, World Peace Foundation, 1934.

21. Nierenstein, M.: Report on the Excretion of Quinine in the Urine, in Observations on Malaria by Medical Officers of the Army and Others, Great Britain War Office, London, His Majesty's Stationery Office, 1919.

22. American Atabrine, Current Comment, J. A. M. A. **120**: 842 (Nov. 14) 1942.

23. Nocht, B., and Mayer, M.: Malaria: A Handbook of Treatment, Parasitology and Prevention, London, John Bale, Sons & Curnow, Ltd., 1937, p. 45.

24. Wats, R. C., and Ghosh, B. N.: Quantitative and Qualitative Methods for Detection of Atabrine in Urine, Rec. Malar. Survey India **4**: 367-370, 1934.

that the needle is in the lumen of the vein. Five-tenths Gm. (7½ grains) of quinine dihydrochloride, or 0.2 Gm. (3 grains) of atabrine may be given as a dose to an adult. To the quinine solution may be added 0.5 to 1 cc. of a 1:1,000 solution of epinephrine hydrochloride. Neither drug should be given more than twice in twenty-four hours. One should guard against collapse.

In an effort to effect still further economies in the consumption of cinchona alkaloids and permit the patient to benefit from both the more rapid action of these alkaloids and the delayed excretion of atabrine, it is now recommended [19] that they be employed consecutively but not concurrently, as was early suggested by Dargan [25] as follows: Give totaquin or quinine as previously suggested for two or three days or until the paroxysms are suppressed, then change to atabrine as previously suggested for five days. If plasmochin is indicated, its administration should await the completion of a five day rest period.

In those falciparum infected patients with a parasitemia exceeding 500,000 parasites per cubic millimeter the prognosis to ordinary therapy is, as has been said,

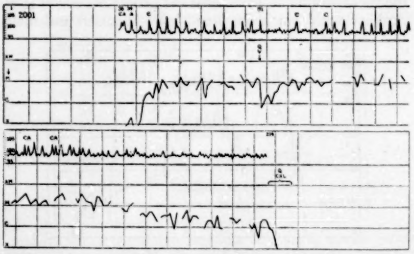

Chart 8.—Naturally induced quartan infection in a white patient. The incubation period required thirty-six days and the prepatent period required thirty-nine days. The onset presented a remittent fever for thirty-six hours and, subsequent to the intermission, changed to a simple quartan intermittent. On the 81st day the administration of 5 grains (0.3 Gm.) of quinine produced a remission lasting eleven days, owing to a depression in the parasitemia. Some irregularities occurred before regular quartan periodicity was restored, and still later a few double quartan paroxysms were noted. Except during the latter period, when some counts slightly exceeded 3,000 per cubic millimeter, very few counts at other times exceeded 2,000 per cubic millimeter. With a gradual spontaneous decline in the parasitemia, the paroxysms diminished in intensity and insensibly ceased. Subsequently 9.3 Gm. of quinine was given in divided doses over eight days.

bad. It is suggested that in addition to the routine therapy these patients may benefit from the mechanical removal of parasites by copious bleeding, the patient at the same time receiving a transfusion of an equal volume of blood from a compatible donor. The amounts removed should be large, totaling a liter or more of blood in twenty-four hours in one or more venesections.

Recrudescences, relapses and recurrences should be treated as suggested for primary attacks. It is frequently difficult to differentiate these from new infections. In some instances differentiation is possible. Thus, if at the clinical onset the parasitemia density is low and enlargement of the spleen is not detectable, a new infection is to be inferred. If on the other hand at the onset the density of parasitemia is appreciable, perhaps even as high as four or five thousand per cubic millimeter, and the spleen is enlarged, one is probably dealing with reactivation of a previously latent infection.

25. Dargan, P. A.: The Therapeutics of Malaria, Indian M. Gaz. 69: 117, 1934.

GAMETOCIDAL THERAPY

Patients with vivax or quartan malaria who are receiving adequate therapy with totaquin or atabrine will have the gametocytes destroyed along with the trophozoites and hence are soon noninfectious. However, those falciparum patients with mature gametocytes still remain infectious while taking adequate doses of these drugs, as the sexual forms are for some reason resistant. Plasmochin, a quinoline derivative, has little action on trophozoites of any species but possesses the unique property of devitalizing the infecting stage of the falciparum parasites, thus making the patient who receives it noninfectious. This constitutes the greatest field for the use of plasmochin. For this purpose it is given in 0.01 Gm. doses three times a day concurrently with each dose of quinine or totaquin during the last five days of the seven day course, or in the same amounts and for the same period, but subsequent to a course of atabrine, an intermission of five days being allowed between the two series. It should be administered after meals. Overdosage with plasmochin will result in the formation of methemoglobin, and the patient will appear cyanotic and may also complain of abdominal pain, sweating or cardiac symptoms. Consequently its administration should be under supervision.

TREATMENT OF LATENT INFECTIONS

Infections may be considered latent (*a*) immediately after therapeutic intervention has produced a remission in an acute attack and (*b*) when parasites are discovered on routine smear examination of an afebrile patient. Such patients often exhibit an anemia and splenomegaly and may find considerable inconvenience from the enlargement of this organ. As long as a patently latent infection is existent it should be borne in mind that recrudescences in falciparum malaria and relapses and recurrences in vivax and quartan malaria are a possibility. While in general unpredictable, yet in vivax infections they unquestionably occur more frequently in the spring. Persons with latent infections may have subclinical rises in their parasitemia and become transitorily infectious and are probably the principal if not the sole factor in maintaining the endemic from one season to the following.

Since the ultimate extinction of a malaria infection probably is more attributable to the activation of the body's immune mechanism than to the administration of the drugs under discussion, the physician faces a problem. Should treatment be protracted in the hope that relapses and recurrences will be prevented or should it be withheld in the expectation that, if there is a renewal of clinical activity, active treatment will be resumed? Opinions will differ and the last word cannot yet be said. In the event that protracted therapy during an induced remission or the treatment of a latent infection is considered indicated, successive courses of atabrine and totaquin should be alternated. In such an event atabrine given as previously described for treatment of the acute attack is administered as the first course, which without delay is followed by a course of totaquin and plasmochin also given as described except that the period over which it is administered is expanded to fourteen days. Each dose of totaquin may be reduced to 0.3 Gm. (5 grains). If further treatment is desirable the courses are repeated, but a rest period of perhaps ten days should intervene between the last day on which totaquin was given and the first day on which the second course of atabrine is begun.

If splenomegaly is persistent, Ascoli and Diliberto [26] advocate the intravenous administration of a protracted course of epinephrine. They begin with 0.01 mg. given daily or on alternate days if the reaction is intense. When any dose is finally supported with little reaction it is gradually stepped up in 0.01 mg. stages until 0.1 mg. is finally given. This is repeated twenty or thirty times until the spleen subsides, which usually happens in about two months. The reaction to the dose is immediate, the patients manifesting pallor, headache, tremors, sometimes psychic and motor excitation, and palpitation.

ABSTRACT OF DISCUSSION

ON PAPERS OF DR. DYER, DRS. HARDY AND WATT AND DR. BOYD

DR. JOSEPH S. D'ANTONI, New Orleans: I am in complete agreement with the substitution by Drs. Hardy and Watt of the definite term shigellosis for the indefinite term bacillary dysentery. The change is logical from the standpoint of etymology and is further justified by the infrequency of dysentery of Shigella origin. I prefer, however, to distinguish more clearly than do the authors between diarrhea and dysentery, because of the possible end results of the two conditions. Whenever dysentery has been present there is a stronger likelihood of permanent bowel dysfunction. A diarrheic stool is a watery stool of fecal composition. A dysenteric stool consists of mucus, blood, cellular débris and pus, the passage of which is always associated with tenesmus. Diarrhea may or may not be interpreted by the patient as an abnormality of intestinal function. Dysentery would be considered abnormal by all patients, regardless of their usual bowel habit. The patients' interpretation of diarrhea and dysentery leads to the question of how many persons with such intestinal disorders consult the physician. A surprisingly large number with diarrhea do not. Of the 380 positive passive carriers of Shigella identified by the authors, only 2 were under the care of a physician, although 38 presently had diarrheal symptoms and 89 were convalescent. One of the group, indeed, was so ill that he died within three days of the survey. One might suppose that any patient with dysentery would seek medical aid at once, but, incredible as it seems, I recall a case of chronic amebic dysentery in a 55 year old Negro who had had from eight to ten bloody stools daily for three years. He claimed that he had not previously come to the hospital, a distance of 3 miles, because he knew he would have to defecate along the way. I am not in complete agreement with the usual impression that passive carriers of Shigella exhibit no clinical symptoms. My experience is that many patients considered as psychoneurotic, who complain of various gastrointestinal symptoms, with or without diarrhea, low grade fever and migratory polyarthritis, frequently, when properly investigated, are found to be suffering from shigellosis. Many of them, if questioned, can recall a previous history of dysentery, and most of them can recall a previous history of diarrhea, though it is true that similar histories might be obtained in any similar selected group of patients. In some cases which I have observed I have identified the same species of Shigella in both the earlier and the later illness, although in the interim the stools were negative and cure had been presumed. The authors' emphasis on repeated stool examinations in shigellosis is entirely correct. My own experience has been that an average of five cultures (using five differential mediums) may be necessary before a diagnosis can be made. It is important to emphasize the necessity of a thorough investigation of all patients with diarrhea who consult the physician. In Shigella infections the diarrhea in the majority of cases is mild and seldom lasts more than three or four days, yet the infection persists long beyond this time. The diagnosis of epidemic diarrheal disease, as the authors point out, is the joint responsibility of the practicing physician and the health officer, and the characteristics of the epidemic furnish the first clue to diagnosis.

26. Ascoli, M., and Diliberto, U.: Therapy of Chronic Malarial Splenomegaly, South. M. J. **25**: 647-649, 1932.

DR. JOSEPH FELSEN, New York: Some idea as to the prevalence of bacillary dysentery may be gained by the fortyfold increase of reported incidence in 1941 as compared with 1933; and the reported incidence is but a fraction of the actual incidence. Diarrheas secondary to primary extraenteric infections are best termed "focal nonspecific enterocolitis," the pathway of bowel involvement being through the indirect hematogenous excretory mechanism. Most positive cultures in acute bacillary dysentery are obtained during the first three days, regardless of the degree of severity. When diarrheal cases in the United States are studied as a group, most of them appear to be bacillary dysentery. Carriers in this disease are "sick" carriers, as revealed by thorough clinical study, including sigmoidoscopy. There is a characteristic three stage progression of pathologic change: punctate follicular hyperplasia, punctate follicular necrosis, and discrete and confluent ulceration on the first, second and third days respectively. These are easily recognizable in the living patient by means of the sigmoidoscope, irrespective of the severity of the disease. The weakest links in the dysentery problem have been the educational and clinical. Prompt isolation, control of food handlers and education of the physician and layman are of paramount importance. Public health officials are concerned with statistical, epidemiologic and bacteriologic studies rather than thorough clinical investigation. A tabulation of epidemiologic data, strains and symptoms is no substitute for careful sigmoidoscopy and clinical acuity. Physicians must learn how to recognize the disease before they can report it. For this reason a clinical classification into the typical and atypical forms (afebrile, asymptomatic, constipated, appendicular, pneumonic, agranulocytoid and meningitic) is most important. Infectivity bears no relationship of severity. In fact, atypical or subclinical forms are often chiefly responsible for the spread of the disease. The Dysentery Registry has proposed as part of its educational program the formation of public health diagnostic teams composed of a suitably trained clinician, bacteriologist and public health worker. I have found sigmoidoscopic crypt aspiration cultures most effective, using a fresh Endo or SS medium. The sulfonamide drugs are a distinct advance but no panacea for bacillary dysentery. More recent advices received from civilian and military sources reveal an increasing number of recurrences and of carriers following the use of the sulfonamides. The absorbed drugs appear to be more effective than those which tend to remain local, the latter being rare in the ulcerated bowel. I again urge vaccination as a prophylactic measure, using endemic strains. Hardy and Watt also noted the protection afforded by a previous attack against subsequent infection with the same strain.

LIEUT. COL. THOMAS T. MACKIE, M. C., A. U. S.: Clinical similarities have rendered classification within the group difficult in the past, and it is only since the application of more exact immunologic methods that the distinction between the four major groups has become evident. Today a sharper distinction may be drawn between the three diseases in the typhus group; European or epidemic typhus, murine or endemic typhus and Brill's disease, and further that Brill's disease and murine typhus are distinct entities. Zinsser, on epidemiologic grounds, originally advanced the theory that Brill's disease represents a recrudescence of an old attack of European or epidemic typhus fever. Recently Plotz, investigating the complement fixation reaction, using unabsorbed and absorbed serums from a group of cases of Brill's disease has obtained strong confirmatory evidence indicating different antigenic patterns in the endemic and epidemic rickettsias respectively. It appears now, therefore, that Brill's disease is in fact a response to the epidemic or European strain in an individual already partially immune from a previous attack of European typhus and that these cases both etiologically and epidemiologically are distinct from the endemic or murine typhus. As Dr. Dyer points out, only two of these diseases, epidemic typhus and tsutsugamushi or Japanese river fever, have military importance. The wide distribution of the latter disease in Southeast Asia and the islands of the Southwest Pacific suggest that it may be a factor in military operations in those areas. Rocky Mountain spotted fever, however, has more immediate interest for the United States in view of its already wide distribution. The investigations on which this classification is

based give promise of the ultimate development of additional methods of control for the entire group of rickettsial diseases, since the identification of immunologically different species constitutes the initial step in the exploration of immunizing vaccines.

BRIG. GEN. JAMES S. SIMMONS, U. S. Army: Rickettsial diseases are actually worldwide in distribution. It is highly appropriate to consider them in a symposium on tropical diseases. At the same time it should be emphasized that their greatest prevalence and most devastating outbreaks have occurred in the more northern regions of the world. Realization of the hazard of typhus to military personnel and civilian groups in war areas and possibly in this country was the basis of the conferences held in the Office of the Surgeon General in August 1942. One important outcome of these conferences was that the President, by executive order number 9285, dated 24 December 1942, established the United States of America Typhus Commission. The work of this commission under the Secretary of War is a joint enterprise of the Army, the Navy and the U. S. Public Health Service. Dr. Dyer has admirably summarized the progress that has been made in recent years in the differentiation of these diseases, in diagnostic methods and in measures for their control by prophylactic vaccination and by the application of new insecticides. There is little to be added to his remarks except by way of amplification from Army experience. The new type Cox vaccine appears to be highly effective. All troops going to typhus areas are vaccinated against typhus. Thus far there have been fewer than 50 reported cases of louse borne typhus in American troops. All these cases have been mild and there have been no deaths. Vaccination against typhus does not prevent infection, but it does modify the disease. The experience of the U. S. A. Typhus Commission accords with this. The advance in the discovery and use of new and effective insecticides has been great, particularly during the years of the war, since 1941. In fact the gains made by military applications of new insecticides against the vectors of insect borne diseases are certain to stand out as some of the most important contributions to the public health and welfare that have been made in recent years. Tsutsugamushi disease, "scrub typhus" or mite borne typhus, regarded formerly by workers in this country as a curiosity, has assumed great military importance because of its prevalence in the Southwest Pacific area and in the China-Burma-India theater of operations. Investigative teams have been sent to those areas to study the disease, its mode of transmission and the mite vector, and to find better methods of prevention. Dimethyl phthalate and other repellents have been found to be effective against Trombicula. Epidemiologic data have been collected from observations of troops in the field. Strains of the causative rickettsia have been brought back to this country for study in several laboratories. From the intensive investigations now being made on tsutsugamushi fever definite and beneficial advances are confidently anticipated.

Diseases Observed in Miners in the Sixteenth and Seventeenth Centuries.—Toward the close of the 16th century and during the early part of the 17th century scattered observations on certain diseases affecting miners had been made by various physicians. Gabriele Fallopius (1523-1562), in his treatise De Meteallis et Fossilibus, noted that the workers in quicksilver mines suffer from mercury poisoning and that the majority of the miners remain at this work for barely three years. Andrea Mattioli of Siena, a contemporary of Fallopius, observed chronic mercurialism among the miners of quicksilver at Idria, in Carniola. Pieter van Foreest (1522-1597) of Delft also made similar observations. J. B. van Helmont (1577-1644), the follower of Paracelsus, in his treatise on asthma and cough, De Asthmate ac Tussi, referred to a variety of asthma peculiar to miners and metal workers. According to Ramazzini, he described "a certain kind of asthma, between the dry and the moist species, which . . . is common among the diggers and refiners of metal, the minters of money, and such other workmen by reason of a metallic gas sucked in along with the air, and which stuffs up the vessels of the lungs.—Rosen, George: The History of Miners' Diseases, New York, Schuman's, 1943.

HEREDITARY SUSCEPTIBILITY IN RHEUMATIC FEVER

THE POTENTIAL RHEUMATIC FAMILY

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At the present time rheumatic fever holds a prominent place in medical discussion and investigation. It is generally agreed that, although the nature of the disease is obscure, susceptibility of the host is the primary factor in the development of rheumatic fever. That this susceptibility is on an age and genetic basis is supported by considerable evidence.[1]

For more than fifty years there has been a widespread clinical impression that heredity is a significant factor in the observed concentration of rheumatic fever in certain families. This belief was based in large measure on the observed familial incidence of the disease. Recent family studies have been in accord with this observation.[2]

Since familial concentration is commonly observed in contagious, dietary and parasitic disorders, a disease may not be considered hereditary on the basis of a high familial incidence alone. Nonhereditary factors must be excluded, and the operation of hereditary factors must be demonstrated by adequate genetic analysis. Genetic and epidemiologic studies have shown that the primary factor responsible for the familial concentration of rheumatic fever is hereditary susceptibility. In a series of rheumatic families studied it was found that the distribution of cases followed the general laws of inheritance. Furthermore, the frequency of cases was consistent with recessive mendelian inheritance.[3]

These studies were limited to a clinic population in New York City. They indicated that, if environmental factors such as climate, living conditions, diet or bacterial agents were responsible for the onset of rheumatic fever in susceptible children, they were uniformly operative and available. It was found that the number of age-genetic susceptibles estimated in every calendar year over a twenty year period of observation was in close agreement with the number of onsets observed. It was also demonstrated that the intrafamilial pattern of spread of rheumatic fever did not exhibit the usual characteristics of a communicable disease. One case did not constitute an obvious risk for secondary cases in the family. Age susceptibility appeared to determine the time of occurrence of cases in the family. It is important to emphasize that, although the number of genetic susceptibles estimated in these families was found to be in close agreement with the final number of cases observed, it cannot be concluded that every genetically susceptible child will necessarily develop rheumatic fever.[3]

The implications of these observations are apparent. The responsibility of the family physician, pediatrician, cardiologist and clinic is not limited to the medical

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1. Wilson, M. G., and Schweitzer, M. D.: Rheumatic Fever as a Familial Disease, J. Clin. Investigation **16**: 555, 1937. Wilson, M. G.: Rheumatic Fever, New York, Commonwealth Fund, 1940, chapter 3, pp. 21-55. Paul, J. R.: The Epidemiology of Rheumatic Fever and Some of Its Public Health Aspects, New York, Metropolitan Life Insurance Company Press, 1943.

2. Cheadle, W. B.: The Various Manifestations of the Rheumatic State as Exemplified in Childhood and Early Life, London, Smith Elder & Co., 1889.

3. Wilson, M. G.; Schweitzer, M. D., and Lubschez, R.: The Familial Epidemiology of Rheumatic Fever: Genetic and Epidemiologic Studies, J. Pediat. **22**: 468 and 581, 1943.

supervision of the rheumatic patient. A complete family history and adequate physical examination of every member of the family are advisable. When it is ascertained that one is dealing with a potential rheumatic family, instructions as to the nature of the disease and its protean manifestations should be given. Until specific preventive measures have been developed, potential susceptibles should be protected from all known predisposing factors which appear to play a role in the onset of the disease. Since the individual susceptible cannot be identified, all the children in a rheumatic family should be under medical supervision. In recessive inheritance eugenic principles are not applicable, unless perhaps in instances when both parents are rheumatic.

If susceptibility to rheumatic fever is transmitted as a recessive character, the chance for each child (in a family or group of families) to be susceptible may be expressed as follows: If both parents are rheumatic, nearly every child will be susceptible. If one parent is rheumatic and the other parent is nonrheumatic but a carrier, i. e. rheumatic fever is present among the immediate family, each child has a 50 per cent chance to be susceptible. If neither parent is rheumatic but both parents are carriers, each child has a 25 per cent chance to be susceptible. (If at least one child is rheumatic, it may be assumed that the negative parents are carriers.) If one or both parents are negative, i. e. definitely known to be nonrheumatic and noncarrier, susceptible children would be unlikely.[4]

The preceding figures may be used to estimate the number of genetic susceptibles present in a family when the genetic constitution of the parents with respect to rheumatic fever is known. If at least one child is known to be rheumatic, the number of genetic susceptibles present in a series of such families may be estimated. Genetic factors have been established which facilitate computation of the number of susceptibles present. It is merely necessary to tabulate the series of families according to family size and multiply each group of families of given size by the appropriate genetic factor. These estimates may then be compared with the actual number of cases of rheumatic fever present in the series.

It is generally believed that the incidence of rheumatic fever is lower in certain sections of the country and infrequent among children of the more favorable economic groups in all sections. Estimation of the role of certain environmental factors may best be made by using the family as the unit for genetic study. For example, if the mortality rates published by the Bureau of Census [5] reflect the relative prevalence of rheumatic fever in various localities, it would be expected that in family studies in certain mountain states where the mortality rate is high there would be close agreement between the number of susceptibles estimated and the number of cases of rheumatic fever actually observed. Similarly, in the south Atlantic states, where the mortality rate is reported to be low, it might be expected that there would be a disparity between the number of susceptibles estimated and the number of cases observed. Such comparisons, made on data accumulated from different geographic locations and diverse economic groups, should yield significant information as to the role of climate and environment in this disease.

Of practical importance is the opportunity afforded for evaluating preventive and therapeutic procedure by making a careful genetic selection of families. Since nearly all the children in families where both parents are rheumatic are probably susceptible to rheumatic fever, even a small series of such families would provide a critical experimental group for study. Recognition and observation of the potential rheumatic family offer a promising field for future research in rheumatic fever.

4. Because of the small size of human families the disease may not be expressed, even though the trait may be present in the family line. One might estimate the probable chance for a susceptible child to be about 3 per cent when one or both parents are negative.

5. Deaths from Acute Rheumatic Fever and Chronic Rheumatic Diseases of the Heart by Age and Race, Each State, 1941, Vital Statistics, Special Reports, United States Department of Commerce, Bureau of the Census, Aug. 18, 1943, vol. 17, No. 31.

CONCLUSIONS

1. The responsibility of the family physician, pediatrician, cardiologist, clinic and school physician is not limited to the medical supervision of the rheumatic patient.

2. The potential rheumatic family should be identified and kept under medical supervision.

3. Studies of potential rheumatic families in different geographic localities and diverse economic groups should yield significant information as to the role of climate and environment in the development of rheumatic fever in susceptible individuals.

4. The public health approach to the control of rheumatic fever, like tuberculosis, may profitably begin with the potential rheumatic family.

CAUSE AND TREATMENT OF FURUNCULOSIS

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The cause of furunculosis is obscure. External spread of bacteria from existing infections to nearby hair follicles is an obvious factor as many writers have pointed out, but that consideration alone does not account satisfactorily for the refractory nature of the disease and its tendency to relapse. Many other causes of furunculosis have been suggested, therefore, such as insanitary personal habits or surroundings, anemia, hypoproteinemia, debility, fatigue, low general or local resistance to the infection, hyperglycemia, low metabolic rate and internal foci of infection. Reflecting this uncertainty of causation, a host of therapeutic measures has been recommended and used for furunculosis, but not one of them has proved uniformly successful.

Certain characteristics of furunculosis point definitely to a local cause for the disease rather than to any systemic abnormality. Furunculosis usually starts with a single infection; thereafter boils tend to appear in succession and not simultaneously in a single crop, as might be expected in a blood borne infection. Furthermore, the individual furuncles invariably begin in hair follicles or their associated sebaceous glands. The lesions are nearly always limited to a region of the body, and extension of the involved area tends to be from the center of that region peripherally. When relapses occur, the infections appear as a rule in the original region. Organisms cultured from different furuncles in the same individual are identical. Not infrequently furunculosis occurs in previously healthy persons in whom no systemic abnormality can be demonstrated. Even during the height of furunculosis, blood culture is almost always negative. These con-

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siderations and a study of the bacteriology of the skin have led to the belief that a local spread of infection is sufficient to account not only for the features just listed but for the characteristic chronicity of the disease as well. Constitutional defects associated with furunculosis are thought to be contributory, secondary or coincidental.

It has been shown [1] that cutaneous bacteria are of two sorts, transients and residents. Transient or contaminating bacteria are loosely attached to the skin surface and are rather easily removed or killed. The resident flora, normally composed of bacteria of slight pathogenicity, is surprisingly stable; it may remain unchanged quantitatively and qualitatively for months or years. This resident flora can be removed or killed only with great difficulty. It is equally difficult to eradicate any particular type of organism which may be included in such a flora. In some way not fully understood certain contaminating bacteria, after prolonged contact with the skin, may change status and become residents. It is thought that, in furunculosis, discharges from the initial lesion carry infectious organisms to the surrounding skin and some of these pathogenic bacteria become incorporated into the resident flora of that region. There they live and multiply, perhaps without harm to the patient until by chance some of them are rubbed deeply into a hair follicle, whereupon a new furuncle starts. With each succeeding furuncle the skin of the region becomes more widely and heavily seeded with the offending bacteria. The fact that these organisms can become part of the resident flora, can live on the skin for long periods of time and are eradicated with great difficulty explains plausibly why furunculosis is so persistent despite local and systemic treatment, and why relapses so often occur in the original site.

Although metastatic infection in bones, kidneys and other distant points is not a rare complication of furunculosis, it occurs in a relatively small proportion of cases. It is probable that pressure, squeezing, incision or other trauma to furuncles produces a transient bacteremia, which in turn results in metastatic abscesses. In my opinion that is an exceptional mode of spread of infection in furunculosis, whereas the usual method of extension is by discharges, sweat, bathing and friction which smear the pathogenic organisms over the skin surface.

If the line of reasoning just presented is correct, rational treatment would consist primarily of an attempt to sterilize the skin of the whole contaminated region. If that could be accomplished, no new furuncles would occur. The word "sterilize" is used here advisedly, since there is reason to believe [1] that pathogenic bacteria in the resident cutaneous flora are no easier to remove or kill than the nonvirulent bacteria which usually predominate on the skin. Any such attempt to sterilize the skin should be carried out without injury to the tissues. And, if possible, subsequent contamination of the area with the same organism should be prevented.

Experimental studies [2] and abundant clinical experience prove that this desired effect cannot be achieved by application of iodine or other strong skin disinfectants. It has been found,[3] however, that healthy skin can be thoroughly degermed with a solution of ethyl alcohol exactly 70 per cent by weight. This particular preparation is a very efficient germicide which does not damage healthy skin even after long contact. Theoretical calculations, based on quantitative studies of skin disinfection, indicate that continuous application of this solution with gentle gauze friction for about twenty minutes will completely sterilize the surface of normal skin. Such treatment should not be used, of course, on open wounds, nor can it be expected to disinfect draining sinuses or hair follicles already deeply contaminated with a boil-producing organism. The optimum time to employ this treatment, therefore, is in the interval between the healing of the last furuncle and the onset of the next one.

In the last ten years many patients with furunculosis have been treated in the manner just described. Eleven of these cases have met the following criteria, and they form the basis of this report: (*a*) All 11 patients had true furunculosis; that is, a more or less continuous succession of deep-seated boils occurring over a period of several weeks or months. (*b*) All had been treated unsuccessfully by other methods. (*c*) All were treated personally by me in accordance with the principles outlined. (*d*) All were followed for two or more years after the alcohol treatment. In all the cases there was complete and usually sudden cure of the condition. And in none of them has there been any recurrence of furuncles during the period of observation.

REPORT OF CASES

The following case histories are typical:

CASE 1.—M. R., a woman aged 30, had been more or less incapacitated by boils on her legs for eight months. Many remedies, including vaccines, yeast, tin, x-rays, chemotherapy and various local applications, had been tried. The infections always began as deep-seated painful indurations, which worked their way slowly to the surface with almost no pus but with necrotic centers which eventually came away, leaving deep craters and relatively large scars. Each boil lasted two to four weeks. They occurred singly and in crops of three or four. Culture showed Staphylococcus aureus. The extremities were unusually hairy. There was no evidence of constitutional disease; the blood sugar and the basal metabolic rate were normal.

Seizing an opportunity when the latest boil had stopped discharging and no fresh ones could be seen, I washed both extremities from the hips to the ankles continuously for twenty minutes with freshly prepared 70 per cent (by weight) alcohol, using light gauze friction. The patient, followed for four years, had no further furuncles.

CASE 2.—M. C., a girl aged 10 years, had not been free from boils for over four months. The infections were scattered over the lumbar region, buttocks and backs of the thighs. Each boil began as a small, rather tender spot followed by a deep, painful induration, a necrotic head, a deep crater and slow healing. Many sorts of treatment had been tried without apparent benefit.

Utilizing a favorable opportunity when a crop of furuncles was subsiding, I placed the patient prone, the genitalia and anus were protected with a heavy coat of petrolatum and the entire infected area was washed with 70 per cent alcohol solution for thirty minutes. No more furuncles appeared, and the patient remained free from them thereafter for at least three years.

CASE 3.—R. C., a boy aged 9 years, had had boils in the region of the right knee for five weeks. When I first saw him 21 healing furuncles and recent scars were counted in an area of about 7 by 4 inches, and a crop of 6 new boils were starting, none of which had come to a head. The boy could not walk because of the pain.

An attempt was made to sterilize the skin at that stage in the manner already described, but evidently it became rein-

1. Price, P. B.: The Bacteriology of Normal Skin: A New Quantitative Test Applied to the Study of Bacterial Flora and the Disinfectant Action of Mechanical Cleansing, J. Infect. Dis. **63**: 301 (Nov.-Dec.) 1938.

2. Price, P. B.: New Studies in Surgical Bacteriology and Surgical Technic, with Special Reference to Disinfection of Skin, J. A. M. A. **111**: 1993 (Nov. 26) 1938.

3. Price, P. B.: Ethyl Alcohol as a Germicide, Arch. Surg. **38**: 528 (March) 1939.

fected with discharges from the six new boils, for subsequently there were additional furuncles and superficial pustules. It was necessary to await a time when the active infections had subsided but before any new infections had started. Such an opportunity presented itself within three weeks. The area was then washed with 70 per cent alcohol for twenty minutes, and this treatment was followed by a complete and permanent relief.

CASE 4.—C. L., a man aged 32, had numerous painful furuncles on the neck, right cheek and chin for sixteen weeks. He had received several x-ray treatments besides local applications of various sorts, staphylococcus toxoid injections and a course of sulfonamide therapy. Zinc iontophoresis was used successfully for some of the infections near the lip.

The long stubble of beard was carefully trimmed away with scissors, and the region was washed gently with 70 per cent alcohol for twenty-five minutes. No more furuncles appeared, and the patient remained free from them for at least three years.

COMMENT

No claims are made for this method of treatment. The number of cases in which it has been used is too small to warrant any final conclusions as to its efficacy. My purpose in this communication is to present a rational theoretical basis for such a treatment together with the results which have been observed to date. It is hoped that wider use of the method will lead to an accurate assessment of its value.

It is important that the alcohol solution should be prepared properly if full disinfectant action is to be obtained. A full discussion of the important differences between percentages by volume and by weight, and directions for preparing 70 per cent alcohol by weight, have been published elsewhere.[2]

The germicidal action of alcohol on the skin is increased by friction, but in the presence of furunculosis rubbing is not without danger. Vigorous massage, particularly when directed against the normal inclination of hair shafts, may actually do harm by pushing live bacteria into hair follicles.

After prolonged application of alcohol the skin feels dry and may itch slightly. Patients should be cautioned not to rub or scratch the region. It is advisable to powder the disinfected area with sterile talcum or zinc stearate. Calamine lotion may be used in selected cases.

It is reasonable to suppose that in the production of furuncles infectious bacteria are first deposited superficially in hair pits, and that they are carried slowly toward the roots of the hairs by natural processes of reproduction and invasion, aided by rubbing, scratching and squeezing on the part of the patient.

I am among those who advocate nonoperative treatment of individual furuncles. Ordinary boils should seldom be incised even when fluctuation is observed but should be permitted to rupture spontaneously. Sinuses should not be dilated and drains should not be inserted. Evacuation of contents by pressure is both unnecessary and dangerous. The temptation to pick out a necrotic core is to be resisted. Caustics such as iodine and phenol applied to a furuncle or its surrounding skin are apt to do more harm than good. During the period of development furuncles may be treated with hot compresses, but they may do equally well if left strictly alone. Rest is important. Just before rupture a sulfathiazole paste dressing may be applied, and this treatment can be used to advantage during the period of discharge. I have had no experience with penicillin, aspergillin and allied compounds in the topical treatment of furunculosis.

It is too early to assess accurately the value of sulfonamides, or of penicillin and related compounds, in the systemic treatment of furunculosis. My impression is that sulfonamides have not been very successful when used for this purpose.

SUMMARY

Regional contamination of the resident flora of skin with boil-producing bacteria is postulated as the primary cause of furunculosis. With that as a working hypothesis a method of treatment has been devised which attempts to eradicate all the offending organisms from the involved area. Eleven patients with furunculosis so treated have had prompt and permanent relief.

OUTBREAK OF SEPTIC SORE THROAT DUE TO RECONSTITUTED POWDERED MILK

EPIDEMIOLOGIC OBSERVATIONS

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AND
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It is well known that most epidemics of septic sore throat are traceable to contaminated raw milk. This, we believe, is the first such outbreak caused by milk from a contaminated "mechanical cow" to be recorded in the literature. As this machine is being widely used to supply our armed forces with fluid milk and ice cream, medical officers should be cognizant of the danger inherent in its improper operation.

CHRONOLOGY OF THE EPIDEMIC

The outbreak studied by us can best be visualized by referring to figure 2, which shows the total number of cases according to the date of onset of symptoms. A total representing approximately 10 per cent of the complement of the station were sick.

A careful inspection of the galley and food handlers was made when it became apparent that an epidemic was starting. Defects noted in the dairy room and preliminary case cards filled out on the first group of patients made it seem probable that milk was the source of the infection, and advice to discontinue its serving was given on the morning of September 30. A rapid subsidence of the outbreak followed compliance with this advice.

Further steps taken to control the outbreak were daily examination of all mess cooks, eliminating those with sore throats. The others were given 1.5 Gm. of sulfadiazine daily as prophylaxis against air borne spread of the disease. As further precaution against upper respiratory spread among the personnel at large, the swimming pool and movie were closed. No other measures were employed.

EPIDEMIOLOGIC EVIDENCE INCRIMINATING MILK

1. Air borne spread was ruled out by lack of correlation between place of work or sleeping quarters and incidence of sore throat.

2. The swimming pool was exonerated, for only 7 per cent of those sick had been swimming in the seventy-two hours preceding the outbreak.

Technical assistance was rendered by J. D. Andrews, PhM 1/c, D. A. Treat, PhM 2/c, J. R. Cook, PhM 2/c, and H. L. Oster, PhM 2/c.
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3. The general mess was indicated as the source, because 100 per cent of the patients had eaten at the mess, whereas several large groups of personnel on the base eating at other messes were not sick.

4. Milk was the only article on the menu statistically significant. Of the first 100 patients admitted to the sick list, 100 gave a history of drinking milk. No other food could be similarly incriminated. Furthermore, inspection of the dairy revealed defects which could easily have allowed the serving of contaminated milk.

BACTERIOLOGIC EVIDENCE OF SOURCE OF INFECTION

A total of 155 throat cultures were made. When samples of these were cultivated on blood agar pour plates they proved to be practically pure cultures of beta hemolytic streptococci (fig. 3). Three of these cultures picked at random were further identified as belonging to group A as determined by the Lancefield precipitin method. Equipment for Griffith subtyping was not available. Cultures from the milk and scrapings from the mechanical cow showed beta hemolytic streptococci.

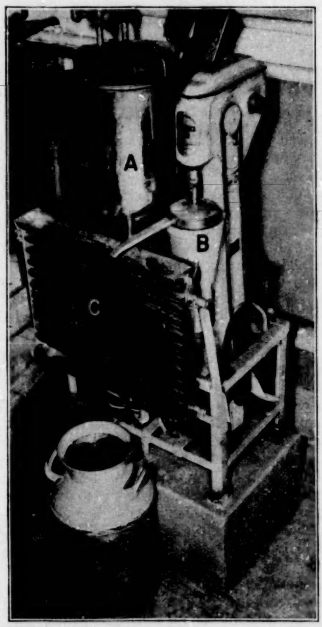

Fig. 1.—Design and operation of the mechanical cow, which is made in 10, 20 and 40 gallon sizes. The required amount of water is placed in the mixing tank (*A*) and heated to 80 F. by allowing live steam to enter the heating jacket surrounding the tank. Powdered dry milk is then sifted into the tank and the mixture agitated for five minutes. The temperature is then raised to 145 F. and held there for twenty minutes. Finally the required amount of sweet cream unsalted butter is added, the complete mixture is agitated for ten minutes while the temperature is kept at 145 F. and then the milk is passed through the high speed emulsifier (*B*). From here it is run over the cooler (*C*), the coils of which should be kept below 38 F. After cooling, the milk can be stored in a refrigerator until ready for use. The mechanical cow is manufactured by the United Dairy Equipment Company, West Chester, Pa.

ULTIMATE SOURCE OF INFECTION

There were two men assigned to work in the milk preparation room. One of them gave a history of having had a sore throat and a tender swollen gland in his neck two weeks before the outbreak. He suffered a recurrence of his sore throat during the epidemic. In spite of the fact that his throat culture was positive for beta hemolytic streptococci, one cannot be certain of the nature of the organism causing his previous sore throat or whether or not he was a carrier.

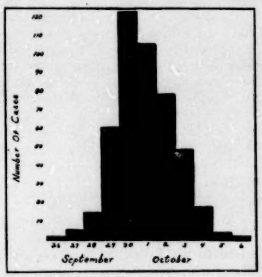

Fig. 2.—Morbidity totals by date of onset. Dispensing of milk was stopped on September 30.

RELATIONSHIP OF PREVIOUS TONSILLECTOMY TO THE MORBIDITY RATE

From the accompanying table it is apparent that there is a positive correlation between the presence of tonsils and one's chances of getting septic sore throat during the course of a milk borne epidemic. The probability that such a distribution could occur by chance as calculated from the formula

$$X^2 = \frac{(ad - bc)^2 (a + b + c + d)}{(a + b)(c + d)(a + c)(b + d)}$$

is less than one in fifty.

Relation of Illness to Presence of Tonsils

	Sick	Not Sick
Tonsils in	77%	56%
Tonsils out	23%	44%

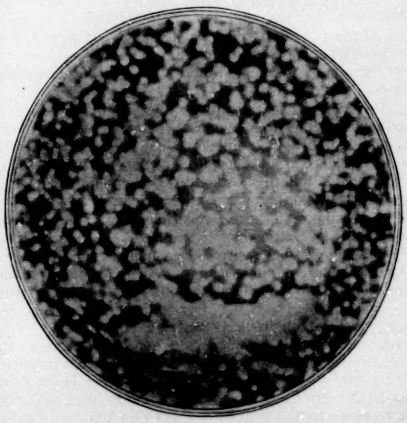

Fig. 3.—Culture of beta hemolytic streptococci.

COMMENT

The chief value of an article such as this is to indicate a new source of danger to the health of military personnel and to recommend means of avoiding this danger

in the future. Based on our experience, the following suggestions are made for the benefit of medical officers at stations or on ships using the "mechanical cow."

1. Foremost in importance is careful instruction of enlisted personnel operating the machine and continued close supervision of their work.

2. Sufficient men should be assigned to the job and an adequate number of "mechanical cows" obtained to supply the needed quantity of milk without having to "railroad it through."

3. A thorough breakdown of the mechanical cow is necessary daily with careful scrubbing of all parts with alkaline washing powder followed by steam sterilization for at least one minute.

4. Weekly checks with a standard thermometer of both the pasteurizing and cooling temperatures is essential. A recording thermometer attached to the mixing tank of the mechanical cow is desirable.

5. Particular attention should be paid to keeping milk cans clean along the seams and prompt retinning of those that rust.

6. Careful screening and adequate ventilation are important and often overlooked items of sanitation.

7. Drying racks for the milk cans of approved construction are easily made and should always be used. Too often cans are placed upside down on the deck.

8. Bulkheads should be kept painted white to encourage cleanliness and expose dirt.

9. Frequent checks on the health of all milk handlers is an important duty of the medical officer.

Clinical Notes, Suggestions and New Instruments

DELAYED MORPHINE POISONING IN BATTLE CASUALTIES

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Early in November 1943 a curious and, as it turned out, a common phenomenon appeared in the operating tents of the forward hospitals: On arrival in the receiving ward the wounded men, many of whom were in shock, all of whom were thoroughly chilled, appeared no different from other such patients. On receiving shock therapy and eventually becoming warmed up, many of these men developed profound respiratory depression associated with pin point pupils, yet neither sign had been present before resuscitation, nor had morphine been administered since arrival in the hospital.[1] These patients clearly appeared to be suffering from morphine poisoning. In the absence of head wounds it was difficult to attribute the condition to anything else.[2]

FACTORS LEADING TO DELAYED TOXIC EFFECTS

Consideration of the circumstances offered a probable explanation for them. In the first part of November it was cold in the valley of the Volturno. It rained, and snow fell low on the mountain sides. If a man was not wet and chilled before being wounded he soon became so after he fell, with the result that the circulation of his skin and subcutaneous region was greatly reduced if not altogether stopped.

It was not likely that morphine administered subcutaneously under these circumstances would be absorbed. Apparently it was not, for in many cases no pain relief occurred following its use, and the first dose of ½ grain (30 mg.) of morphine would be followed by a second or even a third injection over a period of hours, all of these causing little if any effect. In the case of men in good general condition, warming alone with restoration of an active peripheral circulation caused the rapid simultaneous absorption of all the unabsorbed deposits of morphine; in some cases this occurred many hours after the injections had been made. In men in shock, restoration of blood volume and blood pressure, followed eventually by warming, with renewal of the peripheral circulation, led to the seriously rapid absorption of all the morphine injected, and poisoning developed.

In some cases it was necessary to undertake operation before full resuscitation from shock had been accomplished. Here, ether would at first stimulate respiration and then, as the characteristic peripheral vasodilatation occurred, morphine injected many hours before would be rapidly absorbed with development of pin point pupils and profound respiratory depression, before the surgical stage of anesthesia had been reached. In such cases induction of anesthesia was prolonged to nearly an hour.[3]

FREQUENCY OF OCCURRENCE OF THE PHENOMENON

It is impossible to estimate with accuracy the frequency of occurrence of the phenomenon. The complication varies in its manifestations from the hardly perceptible to the fatal. It is often severe enough to be troublesome or serious clinically. In the first ten days of November the syndrome was recognized and pointed out in several hospitals. On the 11th of November it was discussed at the weekly medical meeting of the Fifth Army. Subsequently the phenomenon was everywhere recognized and commented on. It has been found to be a common and at times a serious complication.

It should be emphasized that, although cold weather certainly increased the likelihood of the development of the accident, low blood pressure, surgical shock or any other condition leading to or associated with reduced peripheral circulation presents the possibility for development of the syndrome regardless of the weather. The condition is one to be anticipated in civilian as well as in military practice.

CLINICAL IMPLICATIONS

The clinical implications are concerned with the avoidance of possibility for the development of the syndrome: Whenever possible morphine should be administered intravenously in small doses, ⅛ grain (8 mg.) to ⅙ grain (10 mg.). The full effect is thus achieved in a few minutes, and no possibility for delayed absorption exists. After fifteen or twenty minutes the dose can be repeated if necessary. As a practical matter morphine can rarely be administered intravenously on the battlefield: the extra time required, the necessity for speed, the numbers requiring treatment during heavy action, the frequently collapsed veins of the wounded, the unskilled personnel administering the agent, the poor physical facilities—all of these factors may combine to make necessary the continued use of peripheral injections of morphine. In such cases the injection is made intramuscularly (not subcutaneously) and is followed by massage. The site of the injection is low enough on an extremity so that, if signs of poisoning subsequently develop, a tourniquet can be placed above the morphine deposit in order to slow down the absorption rate. The site of the injection, in addition to the time and size of dose, should be recorded on the man's tag.

When any possibility exists that large unabsorbed deposits of morphine may already be present in a patient, further morphine necessary is administered intravenously in small doses. In such cases morphine is best avoided in preanesthetic medication.

TREATMENT

Realization that morphine intoxication may have a rather abrupt onset many hours after the last morphine injection, under the circumstances discussed, is a considerable help in recognizing the problem at hand. Correct diagnosis leads to prompt and effective treatment. A tourniquet, intermittently loosened, is placed proximal to the site of injection. Primarily the treatment

The surgeon, North African Theater of Operations, U. S. Army, and the surgeon, Fifth Army, gave the author the opportunity to observe and report these findings.

Major Beecher is consultant in anesthesia and resuscitation, North African theater of operations; professor of anesthesia, Harvard Medical School, on leave, and anesthetist-in-chief, Massachusetts General Hospital, Boston, on leave.

1. A similar observation in civil practice (Cocoanut Grove Disaster) is described by Beecher, H. K.: Resuscitation and Sedation of Patients with Burns Which Include the Airway, Ann. Surg. **117**: 825, 1943.

2. Alcohol, chloral hydrate and barbiturates can produce signs similar to those of morphine poisoning but were unlikely complicating factors in the present circumstances.

3. Among other cases, two going on simultaneously in the same operating room showed this sequence, although the last morphine had been injected respectively seven and nine hours before.

of morphine poisoning consists in the effective prevention of anoxia. This is best accomplished by oxygen administration with artificial respiration (if necessary), easily carried out with the aid of a closed anesthesia apparatus by means of intermittent bag pressure, with carbon dioxide absorption. Atropine 1/100 grain (1 mg.) intravenously is probably of value. Ephedrine ½ grain (30 mg.) intravenously has some value as a central stimulant. It will help to support a falling blood pressure. Hypertonic dextrose intravenously is a good diuretic and aids in excretion of morphine by the kidneys. Body heat should be conserved. If coma develops, a gastric tube should be inserted to eliminate the possibility of aspiration of gastric contents. Moreover, frequent change of position is of value in reducing later appearance of pulmonary complications. The treatment is supportive, while the morphine overdose is largely destroyed in the body.

SUMMARY

When the peripheral circulation is sluggish or inactive, as it may be in patients who are chilled or who have low blood pressure, subcutaneous injections of drugs are poorly absorbed. This was frequently observed to be the case in the Italian campaign. Subcutaneous injection of morphine under such circumstances fails to relieve the pain of wounded men. Repeated injections, sometimes over a period of many hours, are not absorbed until finally by shock therapy and warmth the circulation is reestablished in the skin and subcutaneous regions. The unabsorbed deposits of morphine, often totaling a grain or a grain and a half, are then taken up by the active circulation so rapidly that signs of morphine poisoning previously not present then appear, as shock is overcome.

It is usually stated that wounded men require large doses of morphine, doses that may be dangerously large. It is probable that this clinical tradition had at least part of its basis in poor absorption of the morphine in cases such as these. Although the intravenous use of morphine is desirable and would eliminate the problem, such use is not ordinarily practicable under field conditions. In this case, intramuscular injection followed by massage is the choice.

CLOSED REDUCTION OF FRACTURED LUMBAR SPINE WITH UNILATERAL DISLOCATION

LIEUTENANT COLONEL H. B. JENKINS AND MAJOR CHARLES L. NEILL
MEDICAL CORPS, ARMY OF THE UNITED STATES

Fracture dislocations of the lumbar vertebrae are rare. According to Frazier and Allen [1] the infrequency of lumbar dislocations may be attributed to a number of anatomic factors. Unlike the cervical region, where dislocations are most common, there is a comparatively limited range of motion in the lumbar region; the bodies of the lumbar vertebrae are much larger in every dimension; the intervertebral disks are thicker and more elastic; the ligaments at this level of the spine have great strength, and finally—what is probably a factor of greatest importance—the articular processes interlock. These authors have stated that with one exception in all cases dislocations of the lumbar vertebrae have been either backward or forward. In the exceptional case, reported by Schmid,[1] a rotary dislocation is seen in roentgenograms with the second, or proximal, vertebra projected to the right 1.5 cm. beyond the third, or distal, vertebra and the alinement of the spinous processes not disturbed.

In more recent literature Adams [2] reported a case of unilateral dislocation of the fourth on the fifth lumbar vertebra in which there was forward displacement of the spine at the level of the fourth. Attempted reduction by closed manipulation was unsuccessful, and open operation was necessary to correct the deformity. The patient was able to resume normal activities six months later.

A case of fracture dislocation was reported by Barber [3] in which the first lumbar vertebra was displaced laterally on the second and there was considerable anterior displacement. Open operation was necessary to secure reduction. Barber referred to a case reported by Rogers as the only other instance in which open surgical reduction had resulted in satisfactory recovery.

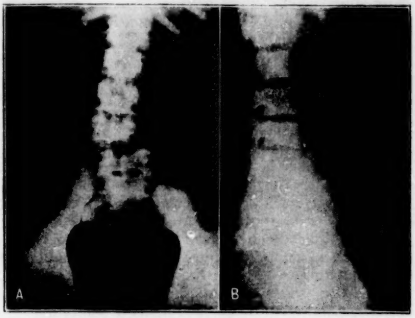

Fig. 1.—*A*, anteroposterior view on admission; *B*, lateral view on admission. Photo by U. S. Army Signal Corps.

A severe crushing fracture of the second and third lumbar vertebrae, with complete lateral and pronounced downward displacement of the first and half the body of the second, was reported by Gordin.[4] There was little evidence of injury to the cord or to the cauda equina, but open operation was done in an attempted reduction, and fragments of lamina, spinous processes and other posterior fragments of vertebrae were removed to prevent eventual pressure of cord or cauda equina due to callus formation. This patient made an excellent recovery with a 2 inch (5 cm.) shortening of the spinal column and side to side union. Six months after injury he was back at work as a laborer.

Böhler,[5] in discussing the treatment of fracture dislocations in the lumbar region, stated that dislocations in the lumbar region could be reduced only by traction or in a bloody way by resection of the processes.

REPORT OF CASE

H. T. T., a white soldier aged 23, native of New York, with eight months' army service, was injured on Aug. 16, 1942

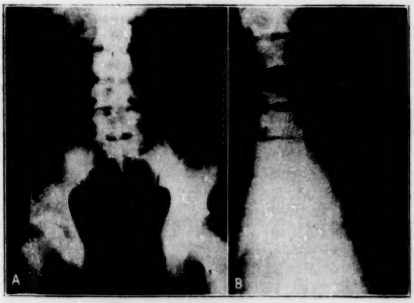

Fig. 2.—*A*, anteroposterior view after closed reduction; *B*, lateral view after closed reduction. Photo by U. S. Army Signal Corps.

when thrown from a truck. He landed on his feet but was knocked down by and pinned beneath the truck, which had

From the Surgical Service of the Station Hospital, Camp Gordon, Georgia.

1. Frazier, Charles H., and Allen, Alfred Reginald: Surgery of the Spine and Spinal Cord, New York, D. Appleton & Co., 1918.
2. Adams, A. Wilfred: Fractured Lumbar Spine with Unilateral Dislocation, Brit. J. Surg. **25**: 632 (Jan.) 1938.
3. Barber, C. Glenn: Open Surgical Reduction of Fracture Dislocation of the Lumbar Spine with Cord or Cauda Equina Involvement, Am. J. Surg. **52**: 238 (May) 1941.
4. Gordin, A. E.: Severe Crushing Fracture of Vertebrae with Complete Recovery, Am. J. Surg. **38**: 374 (Nov.) 1937.
5. Böhler, Lorenz: Wirbelbrüche und Wirbelverrenkungen: Einrichtung von schweren Verrenkungsbrüchen und von Verrenkungen der Wirbelsäule, Chirurg **7**: 643 (Sept. 15) 1935.

overturned. On his admission to the station hospital, Camp Gordon, Georgia, about one hour after the injury, his blood pressure was 116 systolic and 78 diastolic, pulse rate 110, respiratory rate 24 and temperature 98 F. Small lacerated wounds were noted over the right supraorbital region and on the right leg. There was a contused wound over the right iliac crest. There was a complete flaccid paralysis and loss of sensation below the level of the fourth lumbar root distribution on both sides. Roentgen examination revealed a 2 cm. lateral displacement to the left of the fourth lumbar vertebra on the fifth, with fracture of the right inferior articular facet of the fourth and the right superior articular facet of the fifth (fig. 1). After six hours there was slight improvement of sensory function on the left side, but complete loss of motor and sensory function persisted on the right. Eighteen hours after admission there was no further improvement in neurologic function.

With the patient under ether anesthesia on the x-ray table eighteen hours after the injury was incurred, four-man counter-traction on trunk and lower extremities was used, while two-man lateral counterpressure was exerted on the trunk and pelvis, with the fluoroscope being used for observing the reduction. With this manipulation the fourth lumbar vertebra was readily alined, and a plaster spica was applied from the upper part of the thorax to the hips (fig. 2).

The following day pronounced improvement in sensory and motor function was noted. The patient was able to move

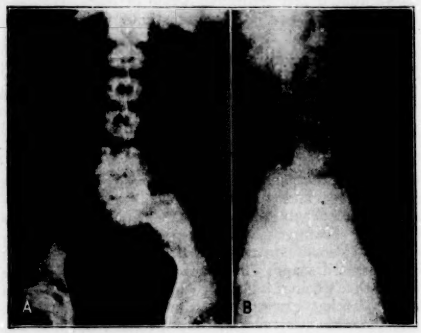

Fig. 3.—*A*, anteroposterior view five months after injury; *B*, lateral view five months after injury. Photo by U. S. Army Signal Corps.

both legs with good muscle power with the exception of the dorsiflexors of the right ankle. There was good touch sensation over both lower extremities, but pinprick sensation was dull over the lateral aspect of the right leg and foot. At the end of two months there were no residual sensory changes and the dorsiflexor muscles of the right ankle were functioning but still weak. There have been no further neurologic changes.

The patient was allowed to go home on a convalescent furlough of thirty days on Jan. 18, 1943, five months after his injury (fig. 3). He was discharged to duty on May 1, 1943, but owing to the weakness of the dorsiflexor muscles of the right foot he was reclassified to limited duty. He now walks without apparent limp, does not have any pain or impairment of movement of the back and has been on continuous active duty as a clerk in the hospital since his discharge as a patient.

SUMMARY

A case of unilateral fracture dislocation of the fourth on the fifth lumbar vertebra without anterior or posterior displacement and with injury to the cauda equina was observed. No similar case has been encountered in the literature. Closed reduction was effected by manipulation, and the patient has resumed his duties as a soldier. A great force is necessary to produce a dislocation in this region, where the structural support of ligaments, muscles and bone is the strongest of any region of the vertebral column.

Council on Pharmacy and Chemistry

REPORT OF THE COUNCIL

THE COUNCIL ON PHARMACY AND CHEMISTRY IS FREQUENTLY ASKED TO CONSIDER FOR ACCEPTANCE SOAPS WITH CLAIMED ANTI-INFECTIVE ACTION. USUALLY THE CLAIMS FOR BACTERIOSTATIC AND BACTERICIDAL VALUE ARE BASED ON SOME INGREDIENT INCORPORATED IN THE SOAP, OCCASIONALLY ON THE OILS AND FATS USED TO PREPARE THE SOAP. MOST OF THE EVIDENCE THAT HAS BEEN PRESENTED TO THE COUNCIL ON BEHALF OF EACH SUBMITTED ARTICLE HAS BEEN LACKING MANY DETAILS WHICH WOULD PERMIT ADEQUATE EVALUATION. WITH THIS THOUGHT IN MIND THE COUNCIL PROPOSED THAT A REPORT BE PREPARED TO PRESENT THE STATUS OF "ANTI-INFECTIVE" SOAPS WITH THE HOPE THAT IN THE PREPARATION CRITERIA WOULD BE SET UP FOR THE GUIDANCE OF MANUFACTURERS AND ALL OTHERS INTERESTED IN THIS SUBJECT. ACCORDINGLY, HARRY E. MORTON, SC.D., DEPARTMENT OF BACTERIOLOGY, UNIVERSITY OF PENNSYLVANIA SCHOOL OF MEDICINE, HAS UNDERTAKEN AN EXHAUSTIVE REVIEW OF THE INFORMATION THAT IS AVAILABLE ON THE GERMICIDAL ACTION OF SOAPS AND HAS CARRIED OUT MUCH ORIGINAL INVESTIGATION; HIS FINDINGS ARE REPORTED BELOW. AT THE CONCLUSION OF DR. MORTON'S WORK DR. JOSEPH V. KLAUDER, PHILADELPHIA, MADE FURTHER STUDIES AND REPORTS THEM IN A DISCUSSION OF DR. MORTON'S INVESTIGATIONS. THE COUNCIL EXPRESSES ITS APPRECIATION OF THE ASSISTANCE PROVIDED BY DRS. MORTON AND KLAUDER AND HOPE THAT THIS REPORT WILL BE OF SOME INTEREST TO, AMONG OTHERS, THE SURGEON, THE INDUSTRIAL PHYSICIAN AND THE DERMATOLOGIST.

AUSTIN E. SMITH, M.D., Secretary.

"GERMICIDAL" SOAPS

I. THE IMPORTANCE OF A CLEAN SKIN, THE ACTION OF SOAPS IN FREEING THE SKIN OF VIABLE MICRO-ORGANISMS, AND METHODS FOR TESTING THE EFFICIENCY OF GERMICIDAL (MEDICATED) SOAPS

The skin not only serves as a mechanical barrier to the entrance of micro-organisms into the body but, according to some investigators, also exerts a lethal action toward many bacteria. Arnold, Gustafson, Hull, Montgomery and Singer [1] in 1930 demonstrated that micro-organisms making up the exogenous bacterial flora of the skin, referred to by Price [2] as "transients," are readily destroyed by the skin. The destruction of those micro-organisms comprising the endogenous flora, or "residents," as Price [2] calls them, is not as great. The destruction of Serratia marcescens (Bacillus prodigiosus) by the skin on the backs of 13 healthy young adults varied from 89 to 99.7 per cent after an exposure of ten minutes. In addition to Serratia marcescens, Escherichia coli, Eberthella typhosa, Salmonella enteritidis and Pseudomonas aeruginosa (Bacillus pyocyaneus) were readily destroyed by the skin on the palmar surface of clean hands; Staphylococcus aureus, Staphylococcus albus and Staphylococcus epidermis albus were destroyed more slowly. Colebrook [3] likewise observed that hemolytic streptococci, Proteus vulgaris, Klebsiella pneumoniae (Friedländer's bacillus) and Escherichia coli rapidly decreased in number when applied to the skin of a finger.

Arnold and his associates [1] pointed out the importance of clean skin to the self-disinfecting power of the skin. They tested the hands of workmen (electricians and plumbers) before and after washing and cleansing their hands at the end of the day for the ability of the skin to destroy Salmonella enteritidis. Dirty skin had very little destructive action on the test organism, whereas, after washing the hands, there was rapid destruction of Salmonella enteritidis. In the study of hemolytic streptococci in normal persons and in carriers, Hare [4] discovered the organisms on

1. Arnold, L.; Gustafson, C. J.; Hull, T. G.; Montgomery, B. E., and Singer, C.: The Self-Disinfecting Power of the Skin as a Defense Against Microbe Invasion, Am. J. Hyg. **11**: 345-361, 1930.
2. Price, P. B.: The Bacteriology of Normal Skin: A New Quantitative Test Applied to a Study of the Bacterial Flora and the Disinfectant Action of Mechanical Cleansing, J. Infect. Dis. **63**: 301-318, 1938.
3. Colebrook, L.: Ministry of Health Interim Report of Departmental Committee on Maternal Mortality and Morbidity: Appendix D. Memorandum on the Sterilization of the Hands, London, His Majesty's Stationery Office, 1930, pp. 122-135.
4. Hare, R.: Haemolytic Streptococci in Normal People and Carriers, Lancet **1**: 85-88, 1941.

the legs of 96 male students in only 7 instances. Of 16 persons who had no hemolytic streptoococci on the skin of the legs, 4 acquired the organisms on an area of the skin purposely left unbathed, 3 during the first week and the fourth after the second week, thus emphasizing again the importance of cleanliness for the normal self-disinfecting power of the skin.

Yeast cells as well as bacteria were found to be removed from the surface of the skin by Cornbleet and Montgomery.[5] Moist areas suffer a depression of their sterilizing powers, and areas with denuded epithelium are not as efficient as intact areas in removing yeasts and staphylococci.

Arnold and his associates[1] noticed that the self-disinfecting power of the skin varied somewhat with different regions of the body, as did Cornbleet and Montgomery.[5] The skin in the nail region of the tips of the fingers was poorer in its self-disinfecting power than the skin on the palmar and dorsal surfaces. There was a slight but constant difference in the self-disinfecting power of the skin on the palmar and dorsal surfaces of the hand (Karns and Arnold[6]). Fisher[7] reported that there was a decided drop in the self-disinfecting power of the skin on the hands of some women during the menstrual cycle.

Many workers have observed that micro-organisms, such as staphylococci, commonly found in the endogenous bacterial flora of the skin often increase in number during washing with soap and water. In a recent article Arnold[8] states that the cornified layer of the skin behaves like a colloidal gel structure; increase in water content causes an increase in the surface endogenous flora, while dehydration is associated with a decrease in the viable bacteria. The flora returns to the normal density when the cornified layer readjusts itself. The endogenous bacterial flora can be increased by alkalization and by exposure to warm water and to warm humid air. It can be decreased by exposing the skin to acid. A cornified layer with increased water content permits exogenous bacteria to survive for longer periods of time; a dehydrated layer rapidly renders the bacteria nonviable.

The only results at variance with the numerous works cited are those of Norton and Novy.[9] The latter workers noticed that the number of bacteria (Serratia marcescens) rapidly diminished after application to the skin. The effect was particularly noticeable during the first ten minutes. Similar results were obtained with inert materials such as glass slides, filter paper and tanned hide. The authors concluded that the most important factor involved was moisture and that living skin did not show any inherent germicidal power. Colebrook[3] attempted to rule out the effect of drying by making comparable tests with broth cultures of various organisms swabbed on fingers and test tubes. Colebrook's results show much less killing of the test organisms on test tubes than on fingers, but the conditions of the tests are not strictly comparable and more and better work could be done profitably concerning this important point.

5. Cornbleet, T., and Montgomery, B. E.: Self-Sterilization Powers of the Skin, Arch. Dermat. & Syph. **23**: 908-919 (May) 1931.

6. Karns, R., and Arnold, L.: Optimum Bacterial Suspension for Testing Skin Disinfection, Proc. Soc. Exper. Biol. & Med. **28**: 375-376, 1931.

7. Fisher, V.: Variations in Self-Disinfecting Power of the Skin During the Menstrual Cycle, Proc. Soc. Exper. Biol. & Med. **28**: 952-953 1931.

8. Arnold, L.: Relationship Between Certain Physicochemical Changes in the Cornified Layer and the Endogenous Bacterial Flora of the Skin, J. Invest. Dermat. **5**: 207-223, 1942.

9. Norton, J. F., and Novy, M. F.: Studies on the Self-Disinfecting Power of the Skin, Am. J. Pub. Health **21**: 1117-1125, 1931.

II. THE ACTION OF SOAPS IN FREEING THE SKIN OF VIABLE MICRO-ORGANISMS

In addition to the esthetic reasons, it has been shown in the preceding section that cleanliness is important for the function of the apparent normal self-disinfecting power of the skin. Soap is usually employed in cleansing the skin because of the readiness with which it removes visible dirt. One of the methods by which soap acts as a detergent is the physical removal of foreign matter, including micro-organisms, owing to its low surface tension. In addition to this physical action, chemical actions may be at work as well. In 1925 Walker[10] stated that the thorough washing of the hands with the formation of a good lather with any ordinary soap was sufficient to destroy any adhering diphtheria bacilli, streptococci and pneumococci. Typhoid bacilli were affected to a lesser extent, and Staphylococcus aureus possessed a pronounced resistance (Walker[11]). The activity of the soap was greatly enhanced by raising the temperature.[12] Colebrook and Maxted[12] in 1933 found that Streptococcus pyogenes was very susceptible to the action of yellow household soap and that staphylococci and Escherichia coli were little affected. Meningococci and gonococci are highly susceptible to the germicidal action of soaps, Walker[13] reporting Neisseria intracellularis killed in an exposure of two and a half minutes by 0.4 to 0.04 per cent solutions of soaps of the fatty acids ordinarily present in soap bases. Neisseria gonorrhoeae was killed under the same conditions by 0.04 to 0.006 per cent solutions of the same soaps. Phenol in 0.5 per cent solution was required under the same conditions. In 1931 Walker[14] added influenza bacilli and Treponema pallidum to the list of micro-organisms susceptible to the bactericidal action of soaps and also reported that meningococci and gonococci were killed in an exposure of two and a half minutes at 20 C. by 1:640 dilutions of white floating soap, coconut oil soap, brown bar (laundry) soap, perfumed soap, Sapo Mollis (U. S. P.) and olive oil soap. The gonococcus was slightly more susceptible, being killed by dilutions of 1:1,280 of white floating soap and coconut oil soap. Colebrook and Maxted observed that refined toilet soaps and soft soap had much less bactericidal effect on Streptococcus pyogenes than yellow household soap.

Soaps prepared from pure fatty acids differed decidedly in their germicidal properties. There was no great difference in the actions of the sodium and potassium soaps of the same fatty acids.[11] Walker[10] stated that the activity of coconut soap against the typhoid bacillus seems to be due to its high content of saturated fatty acids and to the very low proportion of unsaturated acids. In studying the germicidal action of the hydrogen ion and of the lower fatty acids, Cowles[15] concluded that above p_H 2.6 the hydrogen ion concentration rapidly loses its germicidal power for Staphylococcus aureus. In the case of unbuffered lower fatty acids the germicidal action appears to be due to a summation of the effect of the hydrogen ion and of the undissociated molecule. In the case of the higher fatty acids the germicidal action against Staphylococcus aureus

10. Walker, J. E.: The Germicidal Properties of Soap, J. Infect. Dis. **37**: 181-192, 1925.

11. Walker, J. E.: The Germicidal Properties of Chemically Pure Soaps, J. Infect. Dis. **35**: 557-566, 1924.

12. Colebrook, L., and Maxted, W. R.: Antisepsis in Midwifery, J. Obst. & Gynaec. Brit. Emp. **40**: 966-990, 1933.

13. Walker, J. E.: The Germicidal Properties of Soap, J. Infect. Dis. **38**: 127-130, 1926.

14. Walker, J. E.: The Germical and Therapeutic Applications of Soaps, J. A. M. A. **97**: 19-20 (July 4) 1931.

15. Cowles, P. B.: The Germicidal Action of the Hydrogen Ion and of the Lower Fatty Acids, Yale J. Biol. & Med. **13**: 571-578, 1941.

appears to be due mainly to the undissociated molecule. Valette and Liber [16] reported that the germicidal action of the sodium salts of lauric, linoleic and ricinoleic acids on Staphylococcus aureus depended on the degree of hydrolysis. When tested in buffered solutions at p_H 5.8, 6.4, 7.2 and 8.0, sodium laurate and sodium linoleate were most effective at p_H 5.8. Sodium ricinoleate was most effective at p_H 6.4. Considering the p_H of the buffered solutions, it may be inferred that the germicidal action of these compounds is due to the undissociated fatty acid molecule. Colebrook and Maxted determined that it was not the alkalinity of the soap which was responsible for the bactericidal action on Streptococcus pyogenes.

Aside from the ordinary detergent action of soaps due to physical actions, certain micro-organisms appear to be killed by the chemical actions of the soaps. It is quite logical to expect that an attempt would be made to incorporate certain germicides in soaps in order to make the soaps germicidal to a wider range of micro-organisms and perhaps in higher dilutions of the soap. As was pointed out by Hamilton,[17] the incorporating of a germicide in a soap is not without practical difficulties because of the physical properties of the resulting mixture or of chemical reactions impairing the quality of one or both of the two agents. The use of mercuric iodide as proposed by McClintock [18] in 1897 has been used for the longest time and appears to be the most effective germicide after incorporating in soap (Symes,[19] Norton,[20] Colebrook and Maxted [12]).

III. TESTING SOAPS FOR THEIR GERMICIDAL ACTION

As a starting point, the general directions for testing antiseptics and germicides as set forth in Circular No. 198 [21] of the United States Department of Agriculture can be followed for technic, but advantage should be taken of improvements in culture mediums which have been made in recent years. In the case of soaps, changes must also be made in the period of exposure of germicide and test organism. The majority of the germicidal soaps contain mercurials which are known for exerting a very high bacteriostatic, rather than a bactericidal, effect. Shippen [22] recommended transferring four loopfuls from each subculture to a second tube of subculturing medium. This was for the purpose of diluting, to a point where it was no longer bacteriostatic, the germicide transferred to the first subculture tube along with the inoculum. However, this procedure probably does not remove any mercurial compound which may be bound, loosely or otherwise, to the micro-organisms and which may be continuing to exert a bacteriostatic effect. Another possible fallacy of this technic is that after the micro-organisms have been exposed to the germicide for as long as fifteen minutes the number of viable organisms contained in a loopful of material may be so small as not to allow any to be transferred with the four loopfuls of medium from the first subculture tube to the second subculture tube. Also the amount of germicide attached to the bacterial cells might be sufficient to prevent their growth or at least to prolong the lag period beyond the required incubation period of forty-eight hours. This assumption is verified by the results of tests reported in table 1.

The medium proposed by Brewer [23] in 1940 for the cultivation of anaerobic micro-organisms was found also to have the property of destroying the bacteriostatic effect of mercurial compounds which might be present in materials as preservatives, thus preventing the mercurials from continuing to exert a bacteriostatic effect in the subcultures. Sodium thioglycollate medium has been made the approved medium by the National Institute of Health for the testing of biologic products since July 1, 1942. It cannot, however, be considered a universal medium, as McClung [24] reported that it was unsatisfactory for certain members of the genus Clostridium.

The usual precautions that each lot of medium support adequate growth of the test organism should be observed, and in addition it must be demonstrated that each lot of thioglycollate medium is capable of destroying the bacteriostatic effects of mercurial compounds. An inoculum of 1 to 4 cells of Staphylococcus aureus has been found to initiate growth in either extract broth or sodium thioglycollate medium. However, the incubation period of forty-eight hours as prescribed in Circular No. 198 [21] when using extract broth for the subculturing medium is not sufficient when employing the sodium thioglycollate medium. This may not be due to the medium being poor in growth promoting qualities but rather to the fact that thioglycollate medium contains 0.05 per cent agar to make the medium less fluid and reduce convection currents. When only a few viable organisms are present in the inoculum, growth takes place as small discrete colonies, in contrast to the diffuse turbidity which takes place in a tube of extract broth or other fluid medium. Tubes of sodium thioglycollate medium often do not show visible signs of growth until between forty-eight and seventy-two hours, and occasionally between seventy-two and ninety-six hours. Seldom have changes been observed after ninety-six hours of incubation, but they do take place, so it is desirable to incubate subcultures in sodium thioglycollate medium for one week.

Technic.—1. Sterile distilled water was employed in making all dilutions.

2. In the case of liquid soaps, a 5 cc. portion was transferred to the first medication tube and another portion was employed for preparing serial dilutions in the medication tubes. The total volume of soap or soap solution in each medication tube was 5 cc.

3. In the case of bar soap, thin shavings were made from the edge of the bar, weighed on an analytic balance and transferred to a sterile graduated cylinder with a ground glass stopper. Usually the soap shavings were dissolved and diluted to 25 or 50 cc. in a cylinder of 50 cc. capacity. To hasten solution the cylinders of soap solution were frequently placed in a 37° C. water bath for a short time before the serial dilutions were made up.

4. The tests were carried out at room temperature.

16. Valette, G., and Liber, A.: Influence du p_H sur le pouvoir antiseptique des savons et des sels biliaires, Compt. rend. Soc. de biol. **135**: 851-852, 1941.
17. Hamilton, H. C.: Facts and Fallacies in Disinfection, Am. J. Pub. Health **7**: 282-295, 1917.
18. McClintock, C. T.: A New, Practical Disinfectant Material, M. News, New York **70**: 485-487, 1897.
19. Symes, J. O.: The Antiseptic and Disinfectant Properties of Soap, Bristol M.-Chir. J. **17**: 193-197, 1899.
20. Norton, J. F.: Soaps in Relation to Their Use for Hand Washing, J. A. M. A. **75**: 302-305 (July 31) 1920.
21. Ruehle, G. L. A., and Brewer, C. M.: United States Food and Drug Administration Methods of Testing Antiseptics and Disinfectants, Circular 198, United States Department of Agriculture, December 1931.
22. Shippen, L. P.: A Fallacy in the Standard Methods of Examining Disinfectants, Am. J. Pub. Health **18**: 1231-1234, 1928.
23. Brewer, J. H.: Clear Liquid Mediums for the "Aerobic" Cultivation of Anaerobes, J. A. M. A. **115**: 598-600 (Aug. 24) 1940.
24. McClung, L. S.: Thioglycollate Media for the Cultivation of Pathogenic Clostridia, J. Bact. **45**: 58, 1943.

5. A twenty-four hour old culture of Staphylococcus aureus in extract broth p_H 6.8 was employed. It was maintained under conditions described in Circular No. 198. Five-tenths cc. was added to each medication tube.

6. Subcultures were made at intervals of five, ten and fifteen minutes with a 4 mm. platinum loop bent at an angle so that the flat surface of the loop was parallel to the surface of the fluid in the medication tubes when withdrawn. If a soap showed killing action in an exposure of five or ten minutes, it was retested at intervals of one-half, one, two, three and four minutes.

7. The temperature of incubation of subcultures was 37 C.

8. The duration of incubation of subcultures was one week.

9. The growth in critical tubes was checked microscopically and often by streaking onto appropriate medium.

Interpretation of the Results in Table 1.—1. Extract broth is not a satisfactory subculturing medium when testing soaps which contain a mercury compound.

2. The procedure of subculturing the material in the primary subculture tubes to a second tube of extract broth, as recommended by Shippen,[22] is not satisfactory in destroying the bacteriostatic action of mercurial compounds.

3. Subculturing from the medication tubes directly into sodium thioglycollate medium is satisfactory, without making additional subcultures.

4. An exposure of the inoculum-germicide mixture to the action of sodium thioglycollate medium for fifteen minutes appears to be sufficient in the majority of cases to destroy the bacteriostatic action of the mercurial compound.

TABLE 1.—*Comparison of Extract Broth and Sodium Thioglycollate Medium as Subculturing Mediums in Testing Soaps Which Contain Mercurial Compounds*

	Extract Broth for Primary Subcultures									Sodium Thioglycollate Medium for Primary Subcultures								
	5 Min.	A	B	10 Min.	C	D	15 Min.	E	F	5 Min.	A	B	10 Min.	C	D	15 Min.	E	F
Phenol																		
1:80	−	−	−	−	−	−	−	−	−	+	−	−	−	−	−	−	−	−
1:90	+	−	+	−	−	−	−	−	−	+	+	+	−	−	−	−	−	−
1:100	+	+	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+
Neko soap, liquid *	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1:5	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
1:10	−	−	+	−	−	+	−	−	+	+	+	+	+	−	−	−	+	−
1:50	−	+	+	−	−	+	−	−	+	+	+	+	+	+	+	+	+	−
1:100	+	−	+	−	+	+	−	−	+	+	+	+	+	+	+	+	+	+
1:250	+	+	+	−	+	+	−	−	+	+	+	+	+	+	+	+	+	+
1:500	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+
Neko soap, bar †																		
1:50	−	−	+	−	−	−	−	−	−	+	+	+	+	−	−	+	+	−
1:100	−	−	+	−	−	−	−	−	−	+	+	−	+	+	−	+	−	−
1:200	+	+	+	+	−	+	−	−	−	+	+	+	+	+	+	+	+	+
1:400	+	−	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+
Neko soap, bar ‡																		
1:50	−	−	+	−	−	+	−	−	+	+	+	+	+	+	+	+	+	+
1:100	−	−	+	−	−	+	−	−	+	+	+	+	+	+	+	+	+	+
1:200	−	+	+	−	−	+	−	−	+	+	+	+	+	+	+	+	+	+
1:400	−	−	+	−	−	+	−	+	+	+	+	+	+	+	+	+	+	+
1:600	+	−	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+
1:800	+	−	+	−	−	+	−	−	+	+	+	+	+	+	+	+	+	+
Septicide soap, liquid §	−			−			−			−			−			−		
1:5	+			+			−			+			+			−		
1:10	+			+			+			+			+			+		
Metaphen soap, bar ¶																		
1:20	..			..			..			+			+			+		
1:25	+			+			+			+			+			+		

− = no growth; + = growth of the test organism, Staphylococcus aureus.
* Contains 0.25 per cent mercuric iodide.
† Contains 1 per cent mercuric iodide.
‡ Contains 2 per cent mercuric iodide.
§ Contains other germicides in addition to an equivalent of 1:7,000 mercury bichloride.
¶ Contains metaphen 1:500.

Tubes in columns A, C and E were extract broth and tubes in columns B, D and F were sodium thioglycollate medium used for subculturing the primary subcultures. These tubes were inoculated as follows: As soon as the standard phenol coefficient test was completed, 1 cc. from a primary subculture tube, after thorough mixing, was removed with a sterile 1 cc. pipet, 0.5 cc. transferred to a tube of extract broth, labeled either A, C or E, and the remaining 0.5 cc. transferred to a tube of sodium thioglycollate medium, labeled either B, D or F. After the contents of the tubes were thoroughly mixed, the tubes were incubated with the other tubes from the test. By employing the same time schedule as used for the phenol coefficient test and beginning immediately after completion of the test proper, the inoculum in each primary subculture tube was in contact with the subculturing medium for fifteen minutes. Sterile 1 cc. pipets were employed for making the subcultures from the primary subculture tubes instead of transferring 4 loopfuls, because it is more practical, being quicker and the larger inoculum more advisable if only a few viable organisms are present.

5. On the basis of the results with phenol, sodium thioglycollate medium is as satisfactory as standard extract broth for a subculturing medium even in the absence of a mercurial compound. (A word of caution is in order, however, as some lots of sodium thioglycollate medium required inoculums of about ten times the number of organisms necessary to initiate growth in standard extract broth.)

As far as could be learned, the following soaps are on the market which are claimed by the manufacturers to be germicidal:

Liquid Neko (Liquid Germicidal Soap), manufactured by Parke, Davis & Co., Detroit. Contains 0.25 per cent mercuric iodide.

Neko (Germicidal Soap, 1 per cent), manufactured by Parke, Davis & Co., Detroit. Contains 1 per cent mercuric iodide.

Neko (Germicidal Soap, 2 per cent), manufactured by Parke, Davis & Co., Detroit. Contains 2 per cent mercuric iodide.

Septicide Soap (Liquid), manufactured by National Drug Company, Philadelphia. Contains isopropyl alcohol 10 per cent, ether 10 per cent and equivalent of mercury bichloride 1:7,000.

Metaphen Soap, manufactured by Abbott Laboratories, Chicago. Contains metaphen 1:500.

Fawn Soap, manufactured by Fawn Soap Laboratory, Philadelphia. Contains chloramine-T 7 per cent.

The following toilet or household soaps were included in the tests for the purpose of determining the effect on the test organism of an ordinary soap which contains no added germicidal agent:

Fels Naphtha Soap, manufactured by the Fels Soap Company, Philadelphia.

Ivory Soap, manufactured by Proctor & Gamble, Ivorydale, Ohio.

Lifebuoy Soap, manufactured by Lever Bros., Cambridge, Mass.

Cuticura Soap, mildly medicated for toilet, manufactured by Potter Drug and Chemical Corporation, Malden, Mass.

Noxzema Brand Cream Soap, distributed by Noxzema Chemical Company, Baltimore.

Green Soap, obtained from a department of surgery.

Synol, a liquid soap manufactured by Johnson and Johnson, New Brunswick, N. J.

In table 1 are listed the results of the germicidal tests with those soaps containing mercurial compounds which require a special subculturing medium, such as sodium thioglycollate medium, for the purpose of destroying the bacteriostatic action of the mercurial compound. For the other soaps tested, standard extract broth is satisfactory. Results of the tests with soaps other than those listed in table 1 are listed in table 2.

Interpretation of Results in Table 2.—No evidence was observed of killing action against Staphylococcus aureus by the two brands of household soap, by four brands of toilet soap, by Green Soap or by Fawn germicidal soap in the dilutions employed. The dilutions employed in the test are comparable to the concentration of soap in lather.

In addition to taking advantage of the newer knowledge in testing mercurial disinfectants, the conditions under which the compound will have to exert its killing action in actual usage, i. e. time of exposure and concentration of the soap, should be considered. In the standard phenol coefficient test the end point is that dilution of the compound which will kill the test organism in ten minutes' exposure but not in five minutes. During the washing of hands in actual practice, the soap would not be in contact with the skin for a period of time as long as ten minutes. A minute is probably a fair estimate of the length of time a person uses soap in the careful washing of the hands (excluding surgeons). From the results listed in tables 1 and 2, only a few soaps showed killing action in the standard phenol coefficient test. These soaps were retested in shorter intervals of exposure. The results are given in table 3. In testing the germicidal action of soaps, workers have usually employed 1 or 2 per cent solutions of the soaps. A 1:50 or 1:100 dilution of soap will not lather when washing the hands. In actual washing of the hands, if a lather is produced it is a good indication that the concentration of the soap is greater than a 2 per cent solution. Walker [10] stated that the concentration of soap in a good lather is about 8 per cent. In hurried washing it may be as little as 0.3 per cent, and in prolonged washing it may be as high as 20 per cent. Norton [20] estimated the amount of soap used in washing and found that it averaged about 0.5 per cent. The subjects washed their hands in 500 cc. of water, and Norton's figures represent the concentration of soap in the wash water and not in the lather in contact with the hands.

For the most part these findings substantiate those of Walker. The hands were washed with ordinary soap and water and dried. The clean hands were then washed with distilled water and a bar soap until a lather was produced. Sometimes the hands were washed hurriedly and only a light lather was produced. Other times the hands were washed more carefully and a heavy lather was produced. After about a half minute or a minute samples of the lather were collected in tared weighing bottles and dried over phosphorus pentoxide until constant weight. Thin shavings from the bar of soap were collected before the washing process, placed in a tared weighing bottle and subjected to drying in the desiccator along with the samples of lather to determine if there was an appreciable loss of moisture by the soap. The loss in weight was insignificant. The amount of dry residue from the lather indicated that the concentration of soap in samples of lather varied from 10 per cent weight in a light lather to 20 per cent weight in a heavy lather. In testing soaps for their germicidal action they should be tested in concentrations corresponding to that found in lather, i. e. in about 1:5 or 1:10 dilution. The results of the tests with soaps in this range of concentration are listed in table 3.

TABLE 2.—*Germicidal Tests with Soaps Not Containing a Mercurial Compound*

	Extract Broth for Subculturing			Sodium Thioglycollate Medium for Subculturing		
	5 Min.	10 Min.	15 Min.	5 Min.	10 Min.	15 Min.
Phenol						
1:80	—	—	—			
1:90	+	—	—			
1:100	+	+	+			
Synol	+	+	+	+	+	+
1:2	+	+	+	+	+	+
Green soap						
1:10	+	+	+	+	+	+
1:20	+	+	+	+	+	+
Fawn soap						
1:20	..	..	..	+	+	+
1:25	+	+	+	+	+	+
1:30	..	..	..	+	+	+
Lifebuoy soap						
1:15	..	..	..	+	+	+
1:25	..	..	..	+	+	+
Fels naphtha soap						
1:10	+	+	+	+	+	+
1:20	+	+	+	+	+	+
Ivory soap						
1:10	..	..	..	+	+	+
1:20	..	..	..	+	+	+
Cuticura soap						
1:15	..	..	..	+	+	+
1:25	..	..	..	+	+	+
Noxzema soap						
1:20	..	..	..	+	+	+
1:40	..	..	..	+	+	+

— = no growth; + = growth of the test organism, Staphylococcus aureus; .. = test not done. Conditions of the test were the same as described under the heading of Technic.

Interpretation of the Results Listed in Table 3.—Of the soaps tested, only those containing 1 or 2 per cent mercuric iodide killed Staphylococcus aureus in an exposure of one minute, which more nearly represents the time of exposure in ordinary washing of the hands.

Since the bacteriostatic action of mercurial compounds may be neutralized by such substances as sodium thioglycollate, the following experiment was carried out to determine if perspiration is able to neutralize the bacteriostatic action of a mercurial: Perspiration was collected, sterilized by filtering through a sintered Pyrex glass filter and dispensed into test tubes in 1.5 cc. amounts. Various dilutions of Neko bar soap containing 2 per cent mercuric iodide were prepared. The test organism, Staphylococcus aureus, was added in 0.5 cc. amounts to 5 cc. amounts of the

germicide. At five, ten and fifteen minute intervals a loopful of the culture-germicide mixture was transferred to a tube of perspiration, a tube of extract broth, p_H 6.8, and a tube of sodium thioglycollate medium. After the culture-germicide mixture had been in contact with the perspiration for fifteen minutes, 0.5 cc. was subcultured into a tube of extract broth and 0.5 cc.

TABLE 3.—*Germicidal Tests with Soaps in Short Intervals of Exposure and in Concentrations Comparable to Those Found in a Good Lather*

	½ Min.	1 Min.	2 Min.	3 Min.	4 Min.	5 Min.	10 Min.	15 Min.
Neko soap, liquid (0.25% mercuric iodide)	—	—	—	—	—	0	0	0
1:2 dilution	+	+	—	—	—	—	—	0
1:5 dilution	+	+	+	+	—	—	—	—
1:10 dilution	+	+	+	+	+	+	+	—
1:20 dilution	+	+	+	+	+	+	+	+
Neko soap, bar (1% mercuric iodide) 1:5 *	—	—	—	—	—	—	—	—
1:10 *	+	—	—	—	—	—	—	—
1:20	+	+	+	+	—	—	—	—
Neko soap, bar (2% mercuric iodide) 1:5 *	—	—	—	—	—	—	—	—
1:10 *	0	—	—	—	—	—	—	—
1:20	+	+	—	—	—	—	—	—
Metaphen soap, bar (1:500 metaphen) 1:20	+	+	+	+	+	+	+	+
Septicide soap, liquid	+	+	—	—	—	—	—	—
1:2 dilution	+	+	+	+	+	+	—	—
1:5 dilution	+	+	+	0	0	+	+	+

— = no growth; + = growth of the test organism, Staphylococcus aureus; 0 = not tested. Sodium thioglycollate medium used as the subculturing medium. Conditions of the test as described under the heading Technic.

* Very difficult to work with soap in this concentration. The 1:5 dilution was prepared by heating the material in a water bath at 56 C. until solution was attained. After the dilutions were made the tubes were placed in a water bath at room temperature for a few minutes, then inoculated with the culture. The material formed a stiff gel, which made subculturing difficult.

into a tube of sodium thioglycollate medium. The results of the tests are given in table 4.

Interpretation of the Results Listed in Table 4.—Perspiration does not destroy the bacteriostatic action of mercuric iodide contained in soap.

COMMENT

In testing germicidal soaps, as with other germicides, it is necessary to employ a subculturing medium which will destroy the bacteriostatic action of the germicide which, of necessity, is transferred to the medium in the inoculum. In the case of mercurial compounds, sodium thioglycollate medium is satisfactory for this purpose. McClintock [18] realized the importance of neutralizing the mercurial transferred with the inoculum, because in his publication in 1897 he stated that he subcultured from the medication tube to a tube containing ammonium sulfide to precipitate any mercury carried over in the loopful of material and then subcultured to a tube of appropriate medium, a method introduced by Geppert. It appears that this method and that described by Shippen [22] are not as satisfactory as sodium thioglycollate in destroying the bacteriostatic action of mercurial compounds.

It is well to recall the meanings of the terms "disinfection" and "sterilization." The former means the act or process of destroying pathogenic germs or agents and the latter means the act or process of destroying all bacterial life. In either case the destruction is, or should be, an irreversible action. If it is possible to demonstrate that bacteria are viable after the bacteriostatic action of a compound has been neutralized, the bacteria have not been destroyed and the compound cannot be called truthfully a germicide or disinfectant. For scientific reasons the differentiation must be made between bacteriostatic and bactericidal actions. Whether or not pathogenic bacteria, while under the influence of the bacteriostatic action of a compound such as a mercurial, are capable of producing an infection is a point which was not investigated.

By the heretofore accepted methods of testing germicides some of the germicidal soaps, especially the brands of soaps containing mercuric iodide, appeared to possess high germicidal powers. It has been observed repeatedly that the test organism Staphylococcus aureus appears to be killed by a 1:800 dilution of Neko soap containing 2 per cent mercuric iodide in an exposure of ten minutes. When sodium thioglycollate medium is employed as the subculturing medium the same soap in a 1:50 dilution fails to kill in an exposure of fifteen minutes. The liquid Neko soap, containing 0.25 per cent mercuric iodide, kills Staphylococcus aureus in an exposure of five minutes when diluted 1:5 and in a ten minute exposure when diluted 1:10 when subculturing into sodium thioglycollate medium. When subculturing into extract broth it appears that the organisms are killed in an exposure of five minutes in a dilution of 1:50 and in ten minutes by a 1:250 dilution of the soap.

Symes [19] recommended McClintock's soap, containing 2 per cent mercuric iodide (Neko) as a useful means of disinfecting hands, instruments and surfaces, but after examining the results in table 1 one can see that Symes was basing his recommendations on the bacteriostatic rather than on the bactericidal action of mercuric iodide. He failed to distinguish between these two modes of action of mercurials.

Septicide liquid soap, when undiluted, killed the test organism in an exposure of five minutes, but an exposure of fifteen minutes was required to kill the test organism when the soap was diluted 1:5. The same killing power was obtained whether the subcultures were made in extract broth or in sodium thioglycollate medium, indicating that it was not the mercurial in the soap which was responsible for the killing action. Birkhaug [25] observed that a 1:14,000 dilution of mercury bichloride was needed to kill Staphylococcus aureus in ten minutes' exposure but not in five minutes when subcultures were made in extract broth. Nye [26] obtained values between 1:8,000 and 1:16,000, and Ecker and Smith [27] reported that a 1:5,000 dilution was needed for killing in the same time interval. When subcultur-

TABLE 4.—*The Effect of Perspiration on the Bacteriostatic Action of Mercuric Iodide*

(Neko bar soap, containing 2 per cent mercuric iodide)

Dilution of Neko Soap	5 Minutes' Exposure Perspiration				10 Minutes' Exposure Perspiration				15 Minutes' Exposure Perspiration			
	B′	T′	B	T	B′	T′	B	T	B′	T′	B	T
1:50	—	—	—	+	—	—	—	+	—	—	—	+
1:100	—	—	—	+	—	—	—	+	—	—	—	+
1:200	—	+	—	+	—	+	—	+	—	—	—	+
1:400	—	+	—	+	—	—	—	+	—	+	—	+
1:800	—	+	—	+	—	+	—	+	—	—	—	+

— = no growth, + = growth of test organism, Staphylococcus aureus. B = subculturing medium, extract broth p_H 6.8. T = subculturing medium, sodium thioglycollate medium. B′ = culture-soap mixture in contact with perspiration for fifteen minutes before subculturing into extract broth p_H 6.8. T′ = culture-soap mixture in contact with perspiration for fifteen minutes before subculturing into sodium thioglycollate medium.

25. Birkhaug, K. E.: Metaphen (4-Nitro-3, 5 Bisacetoxymercuri 2-Cresol): I. A Comparative Study of Commonly Used Disinfectants and Antiseptics; II. Histologic Changes Produced by the Intravenous Administration of Metaphen in Rabbits, J. A. M. A. **95**: 917-923 (Sept. 27) 1930.

26. Nye, R. N.: The Relative In Vitro Activity of Certain Antiseptics in Aqueous Solution, J. A. M. A. **108**: 280-287 (Jan. 23) 1937.

27. Ecker, E. E., and Smith, R.: Time-Killing Concentrations of Various Mercurials, Mod. Hosp. **48**: 90-94, 1937.

ing into sodium thioglycollate medium it was found that mercury bichloride cannot be diluted beyond 1 : 1,000 and still kill all Staphylococcus aureus organisms in ten minutes. Hoyt, Fisk and Burde [28] reported that less than a 1 : 1,000 dilution was required to kill in the same interval of time.

It is rather easy to test the germicidal action of liquid soaps in vitro. The testing of solid soaps is more difficult, because usually a dilution of the soap much more concentrated than a 1 : 50 dilution forms a gel too stiff for practical purposes of testing by the accepted technics. The dilution of a soap which lends itself well to manipulation with the platinum loop may not correspond to the concentration of the soap in contact with the skin during washing. The use of the agar cup method (Ruehle and Brewer [21]) as described for materials for which it is not practical to obtain aqueous solutions is not to be recommended for use with soaps, because it represents constant exposure of the test organisms to the germicide and because it does not differentiate between the bacteriostatic and bactericidal actions of the germicide. The filter paper technic, also described by the same authors,[21] likewise does not appear to be applicable to the testing of soaps, because if a soap forms a solution sufficiently fluid to wet a piece of filter paper it is fluid enough to transfer with the standard loop.

The usual controls should not be neglected: 1. A knowledge of the resistance of the test organism to phenol is necessary. 2. It should be known that the culture medium supports growth of the test organisms when inoculated with very few of the test organisms. 3. In addition to the culture medium adequately supporting growth of the test organism, the medium should be efficient in destroying the bacteriostatic action of the germicide. 4. It is desirable to inoculate a loopful of diluted culture into tubes of the subculturing medium containing a loopful of the soaps in the highest concentration tested. The diluted culture should be prepared by adding 0.5 cc. of the test culture to 5 cc. of sterile distilled water (the same as used for preparing the dilutions of the soap) and allowing it to remain in contact for fifteen minutes or the longest time interval employed in the test. 5. It is often desirable to inoculate with a standard loopful of the diluted culture described in 4 the subculture tubes which do not show growth at the end of the incubation period. This is especially true of those tubes inoculated from the most concentrated solution of the soap. 6. When employing culture mediums containing small amounts of agar to reduce the fluidity of the medium, it is necessary to lengthen the incubation period. An incubation period of one week has been found to be adequate.

It has been recognized by many investigators that Staphylococcus aureus is very resistant to the action of soaps (Walker [11] and Colebrook and Maxted [12]). Staphylococcus aureus is the most important pyogenic micro-organism, so for all practical purposes it is the best test organism for testing the germicidal action of soaps.

In addition to determining the germicidal action of a soap against certain test organisms in vitro, the direct action in disinfecting the skin can be determined in a manner proposed for the evaluation of skin disinfectants, which have been summarized briefly in THE JOURNAL, Feb. 20, 1943, page 593. An in vivo method for evaluating skin disinfectants was described by Kempf and Nungester,[29] in which the tail of a living animal is contaminated with living micro-organisms virulent for the animal, treating with the disinfectant, snipping off the end of the tail, inserting it into the peritoneal cavity of the animal and observing whether or not infection takes place. Another in vivo method was described by Sarber.[30] It differs from the foregoing method mainly in that a piece of skin from an area on the abdominal wall after being contaminated with living virulent micro-organisms and treated with the germicide is inserted into the peritoneal cavity of the same animal. For determining the action of germicidal soaps on the resident or endogenous bacterial flora of the skin the quantitative method described by Price [31] may be employed and mathematical analysis as suggested by Bernstein [32] applied.

Not only should germicidal soaps be free from irritating and toxic action on skin, mucous membranes or denuded areas, but certain actions on the skin, as suggested by Cromwell and Leffler [33] and Arnold [8] must be borne in mind.

COMMENT BY JOSEPH V. KLAUDER, M.D.

An important practical feature in relation to these studies of the germicidal action of soap is the concentration of soap used in washing the skin. A 1 to 2 per cent solution of soap when employed for hand washing does not lather, yet a detergent action is apparent. Soap is not very soluble—a concentration much above 2 per cent at normal temperature jells and is not usually employed in ordinary hand washing. A higher concentration of soap used in hand washing is attained in the form of lather. To obtain a good lather, the act of washing with soap compound must be prolonged. The concentration of soap solution, the degree of lather and the time of exposure were pertinent factors in germicidal action of those soaps observed to exert such action.

Since soaps containing mercuric iodide exerted germicidal action, discussion of the effect of mercuric iodide on the skin is pertinent. Mercury and nickel are the two notable metals that have allergenic properties. Of the two, nickel has a higher allergenic index. The allergenic index of mercury is not high, certainly not sufficiently high to constitute an obstacle in the routine use of mercurial compounds on the skin. Ammoniated mercury ointment, for example, is frequently used. A person sensitized to mercury may be seen by the dermatologist perhaps once in a few years, among a large clientele, both clinic and practice.

To determine the primary irritant action of mercuric iodide on the skin, patch tests were performed with dilutions up to 2 per cent. Dilutions exceeding 2 per cent were not studied, since that was the maximum concentration of the chemical in the soaps studied in this report. Since mercuric iodide is not soluble in water, patch tests were performed with the chemical dissolved in 3 per cent solution of sodium thiosulfate. This percentage of sodium thiosulfate is not an irritant to the skin. It was observed that the skin of normal persons did not react to 2 per cent mercuric iodide in 3 per cent solution of sodium thiosulfate.

28. Hoyt, A.; Fisk, R. T., and Burde, G.: Antibacterial Action of Certain Disinfectants, Surgery **12**: 786-790, 1942.

29. Kempf, A. H., and Nungester, W. J.: An In Vivo Test for the Evaluation of Skin Disinfectants, J. Bact. **43**: 49-50, 1942.

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31. Price, P. B.: Ethyl Alcohol as a Germicide, Arch. Surg. **38**: 528-542 (March) 1939; The Bacteriology of Normal Skin.[5]

32. Bernstein, L. H. T.: Standardization of Skin Disinfectants, J. Bact. **43**: 50-51, 1942.

33. Cromwell, H. W., and Leffler, R.: Evaluation of "Skin Degerming" Agents by a Modification of the Price Method, J. Bact. **43**: 51-52, 1942.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, APRIL 22, 1944

CRITERIA FOR RECOGNITION OF SHOCK

The common factor in the production of shock is a discrepancy between the effective circulating blood volume and the actual volume capacity of the vascular bed. The development of this fundamental change is primarily responsible for the impressive clinical symptomatology with low temperature, feeble and rapid pulse, cold skin, exhaustion and lowered arterial pressure. However, when this clinical syndrome appears, shock is often irreversible and therapy ineffective. Hence it becomes necessary to establish clinical criteria which will express the earliest, asymptomatic phase of the disparity between blood volume and vascular bed.

Many clinicians still believe that a low or falling arterial pressure constitutes an early and obligatory feature of shock. Blalock,[1] Moon,[2] Harkins [3] and others have repeatedly pointed out that arterial pressure is a completely inadequate guide to the state of circulatory deficiency in incipient shock. Frequently the reactive vasoconstriction leads to an elevation of arterial pressure in the early stages of shock. A low blood pressure would follow later as a sign of advanced decompensation. This may account for the rare incidence of shock found by some investigators [4] in head injuries and some other conditions when blood pressure is used as the only criterion of shock. Moreover, lowering of the arterial pressure may be maintained for several hours, without serious impairment to the circulation, as recently shown by Phemister and his co-workers.[5] An opposite point of view regarding the value of blood pressure readings in shock has recently been expressed by Evans and his associates,[6] who concluded that, as compared with hemoconcentration and blood volume, the blood pressure level was the most valuable sign for early diagnosis of clinical traumatic shock in which hemoconcentration does not occur.

Hemoconcentration is probably the most frequently used single factor for recognition of shock. According to Moon it constitutes the earliest detectable manifestation of shock as well as the most accurate index of its severity. Mainly on the basis that absence of hemoconcentration expresses normal capillary permeability, this worker contends that hemorrhage should be differentiated from shock, as hemorrhage is accompanied by hemodilution and only terminally may be associated with hemoconcentration. In contrast to this concept, Blalock [7] has shown that an irreversible typical syndrome of shock with pathologic signs of increased capillary permeability, which is as a rule associated with hemoconcentration, may be elicited by simple and slow removal of blood. Davis [8] also observed identical pathologic features in protracted hemorrhage and in traumatic shock. Much of the experimental work being done on shock employs the withdrawal of blood as the initiating factor thus implying that the differentiation between shock and hemorrhage has not been generally accepted. Harkins summarizes this point of view, stating that a differentiation between hemorrhage and other types of shock would not have any diagnostic, prognostic or therapeutic value. In clinical cases, often both whole blood and plasma are lost. Hence hemoconcentration is not a regular feature and, except in cases of burns, cannot be relied on as an accurate sign for recognition of early clinical shock.

As the basic disturbance in all types of shock is a reduced blood volume, this estimation could be regarded as the most logical index of impending shock. The determination of blood volume was made feasible in practice by the use of Evans' blue dye. However, the reports on the use of this method in shock provide conflicting results. Although recognizing the significance of reduced blood volume, Freeman [9] has objected to this method because the increase in capillary permeability in shock permits a considerable amount of dye to escape from the circulation. Evans and his associates found, however, that the rate of dye disappearance was the same in normal and in shocked animals. Even if this conclusion is correct, determination of blood volume would not be adequate for following the progress of

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2. Moon, V. H.: Shock and Related Capillary Phenomena, New York, Oxford University Press, 1938.
3. Harkins, Henry N.: Recent Advances in the Study and Management of Traumatic Shock, Surgery **9**: 231 (Feb.) 1941.
4. McGregor, Lee: Head Injuries: A Critical Analysis of 500 Cases, Internat. Abstr. Surg. **75**: 1, in Surg., Gynec. & Obst., July 1942.
5. Phemister, Dallas, B., and others: Afferent Vasodepressor Nerve Impulses as a Cause of Shock, Tested Experimentally by Aortic Depressor Nerve Stimulation, Ann. Surg. **119**: 26 (Jan.) 1944.
6. Evans, Everett I., and others: Studies on Traumatic Shock: I. Blood Volume Changes in Traumatic Shock, Ann. Surg. **119**: 64 (Jan.) 1944.
7. Blalock, Alfred: Shock: Further Studies, with Particular Reference to the Effects of Hemorrhage, Arch. Surg. **29**: 837 (Nov.) 1934.
8. Davis, Harry A.: Factors in the Production and Treatment of Shock: An Experimental Study, M. Ann. District of Columbia **6**: 344 (Dec.) 1937.
9. Freeman, N. E.; Freedman, H., and Miller, C. C.: The Production of Shock by the Prolonged Continuous Injection of Adrenalin in Unanesthetized Dogs, Am. J. Physiology **131**: 545 (Jan.) 1941.

shock since this estimation could not be repeated at frequent intervals.

All other criteria, such as low venous pressure, acapnia, increased cardiac output and rise in blood potassium, are equally unreliable, inconsistent or unpractical for the early characterization of shock. A combination of the commonest manifestations and features, particularly those most suitable for practical use, constitutes a more adequate procedure in the detection and follow-up of different stages of shock. In a certain proportion of cases, peripheral collapse will progress unrecognized until a stage of irreversible circulatory deficiency has developed. The paucity of our present knowledge on this important subject indicates urgent need for further work.

VARIATIONS IN PHAGOCYTIC FUNCTIONS

Studies of vitamin deficiencies have shown that adequate amounts of most vitamins are essential for normal resistance to infectious diseases.[1] Attempts to determine the mechanism by which resistance is lowered in the presence of vitamin deficiency, however, have been unsuccessful. Data thus far reported indicate that antibody response is practically normal in vitamin deficient animals, suggesting the probability that the observed reduction in resistance is due to reduced phagocytic functions.

Careful quantitative studies of variations in phagocytic power under different nutritional conditions have been undertaken by Cottingham and Mills[2] of the Laboratories of Experimental Medicine, University of Cincinnati. In their tests a standard dose of Micrococcus candidus was injected intraperitoneally into mice that had been maintained for several weeks on various partially deficient diets. Four hours later, smears were made of the peritoneal exudates. In a typical test control, mice were maintained at 68 F. for three weeks on a diet containing 2 mg. per kilogram of thiamine, which is adequate for this species. The four hour peritoneal smears showed that 33 per cent of the mononuclear cells had ingested the microorganisms. This degree of phagocytosis was reduced to 20 per cent in mice previously maintained on but 1 mg. per kilogram of thiamine. Phagocytosis was not demonstrable in mice maintained for the same period of time on a diet containing as little as 0.5 mg. per kilogram of thiamine. When the thiamine intake was increased above the growth optimum (2 mg. per kilogram) mononuclear phagocytosis increased to 37 per cent. In the same animals intraperitoneal polymorphonuclear phagocytosis was reduced one half by thiamine deficiency and increased fourfold as a result of thiamine excess (8 mg. per kilogram).

Parallel studies of phagocytosis were made in vitro with the heparinized whole blood of rats which had been maintained for several weeks on deficiency diets. In these tests blood smears were made at the end of four minutes to determine the percentage of cells showing immediate phagocytosis, and at the end of one hour to show evidence of intracellular bacterial digestion (loss of staining power, fragmentation and so on). The investigators found that rats maintained for seven weeks on a diet containing 4 mg. per kilogram of pyridoxine yielded blood whose leukocytes took up an average of 13.56 micro-organisms per cell by the end of four minutes. By the end of one hour 82 per cent of these cells showed evidence of intracellular digestion. On a partial deficiency diet (0.5 mg. per kilogram of pyridoxine), phagocytosis was reduced to 4.95 micro-organisms per cell, and intracellular digestion was demonstrable in but 15 per cent of the phagocytes. Similar or even larger reductions in phagocytic functions were noted in rats fed a diet partially deficient in thiamine, riboflavin, pantothenic acid, choline or combined vitamins A and D. Deficiencies in inositol and p-aminobenzoic acid were without deleterious effects.

Since rats and mice synthesize ascorbic acid, tests of vitamin C deficiency were made on guinea pigs. Leukocytes of adequately fed guinea pigs would take up an average of 18.3 micro-organisms per cell in vitro, and 99 per cent of these cells showed evidence of bacterial destruction by the end of one hour. On a vitamin C deficient diet, phagocytosis was reduced to 7.3 bacteria per cell, with intracellular digestion reduced to 74 per cent.

The Cincinnati investigators supplemented this study by testing the deleterious effects of quantitative variations in protein intake.[3] They found that after five and one-half weeks maintenance at 68 F. rats showed a maximum phagocytic activity on diets containing 18 per cent of protein. There was a definite decrease in phagocytic activity with an increase or decrease from this level. In rats maintained at 90 + F. the phagocytic optimum diet was 36 per cent of protein. Thus adequate protein intake would seem to be fully as important as adequate vitamin intake to maintain optimal phagocytic activity (resistance to microbic infections). The immunologic optimum protein intake is higher in the tropics than in temperate climates.

This demonstration of important variations in phagocytic functions is a pioneer contribution to basic immunologic theory and may have wide clinical implications.

1. Robertson, E. C.: Medicine **13**: 123 (May) 1934. Clausen, S. W.: Physiol. Rev. **14**: 309 (July) 1934.
2. Cottingham, Esther, and Mills, C. A.: J. Immunol. **47**: 493 (Dec.) 1943.
3. Mills, C. A., and Cottingham, Esther: J. Immunol. **47**: 503 (Dec.) 1943.

Current Comment

CRITICAL SHORTAGE OF QUINIDINE

For some time an acute shortage of quinidine has existed in the United States. Consumption has been high and replacement of present supplies practically negligible. As a result of its critical status, the Committee on Drugs and Medical Supplies of the National Research Council and its Subcommittee on Cardiovascular Diseases recommended that quinidine be limited to prescription use for the treatment only of heart disease. The suggested criteria for use are:

1. Ventricular tachycardia diagnosed electrocardiographically.
2. Congestive heart failure that appears definitely to have been precipitated by the sudden onset of auricular fibrillation (if not adequately controlled by digitalis).
3. Persistent premature ventricular contractions in patients who have acute coronary artery occlusion.
4. Chronic disease of the heart associated with paroxysmal auricular fibrillation, paroxysmal auricular tachycardia or auricular flutter.
5. A history of systemic embolization in a case of paroxysmal or established auricular fibrillation.

Regardless of these proposals and the publicity given to them, consumption of quinidine has continued to be high. Ordinarily, about 80,000 ounces of the drug is used during a year; present stocks amount to between 29,000 and 30,000 ounces. It is the duty of every physician to prescribe quinidine only when no other drug will elicit a favorable response, and then only in quantities not exceeding fifty tablets for each prescription. Hospital administrators can provide much assistance by insisting that the members of the staff adhere rigidly to a program which provides for the restricted use of such critical drugs as quinidine. Pharmacists have a moral responsibility to release quinidine only on prescription. This is an emergency, and whole hearted cooperation is essential.

HEALTH TRANSCRIPTION BROADCASTING IN ARIZONA

The Arizona State Medical Association, using electrical transcriptions of the series Before the Doctor Comes, originated by the Bureau of Health Education of the American Medical Association, has developed an excellent continuity. The broadcast is called "The Medical Quarter Hour." The transcription itself occupies only ten minutes, so the program is opened with a familiar theme, for which a popular waltz record is used. Then follows an announcement to the effect that the stations of the Arizona network "present at this time a transcribed public service broadcast made available through the sponsorship of the Arizona Medical Association." Introductory remarks are made by the announcer, who describes the purpose of the broadcasts and gives forecasts of the programs to come. The transcription is then introduced and played. After the transcription, a message is read from the Arizona Medical Association which invites the listeners to send in comments and suggestions and offers to answer questions suggested by the broadcast. If time permits, a Health Hint appropriate to the program is added. For example, in connection with the transcription dealing with "Sniffles" there are some suggestions pertinent to colds and other related conditions. This combination of music, local material and a transcribed message from the American Medical Association is the kind of use for which the transcriptions were originally prepared. This way of giving radio listeners health information from the American Medical Association through community and state societies automatically makes clear the relationship between the family doctor and the medical organization to which he delegates many of his important functions, including health education. The Arizona broadcasts are described here with the thought that this method may contain suggestions for similar use of the available transcriptions in other localities.

THE TRINIDAD OUTBREAK OF EQUINE ENCEPHALOMYELITIS

Equine encephalomyelitis in Venezuela and Colombia is a mosquito transmitted infection caused by a virus that is related to equine neurotropic viruses in this country but immunologically distinct. In October 1943 an explosive outbreak of encephalomyelitis attacked horses, mules and donkeys in the island of Trinidad, 6 miles off the Venezuelan coast at the nearest points. According to Gilyard,[1] who investigated the Trinidad outbreak, there is good reason to conclude that it was due to mosquitoes flying across from the mainland. The prime vector of the epizootic may have been the mosquito Mansonia titillans, but other species cannot be definitely excluded. The virus was obtained from M. titillans in the field on guinea pig inoculations, and Venezuelan vaccine gave complete protection. In addition to the account of the mosquito conveyance of the disease, Gilyard reports also a human case of Venezuelan encephalitis. About six weeks before the equine outbreak a seaman of the U. S. Navy died of encephalitis on the gulf coast of Trinidad about 20 miles north of the subsequent animal outbreak. Just how this seaman was infected is not known, but the diagnosis of equine encephalitis was confirmed by appropriate tests of the brain. This appears to be the first human case in which death has been traced to equine encephalitis of the Venezuelan type. It seems to be established that the three strains of equine encephalitis now known to exist in the Western Hemisphere can cause fatal infections in man.

THE DISTINGUISHED SERVICE MEDAL

The Distinguished Service Medal of the American Medical Association will be presented for the seventh time at the Opening General Meeting on Tuesday night, June 13, in the ballroom of the Palmer House, Chicago, during the annual session of the American Medical Association in Chicago, June 12-16, 1944. The medal was awarded, for the first time, in 1938 to Dr. Rudolph Matas of New Orleans, in 1939 to Dr. James B. Herrick of Chicago, in 1940 to Dr. Chevalier Jackson of Philadelphia, in 1941 to Dr. James Ewing of New

1. Gilyard, R. T.: Mosquito Transmission of Venezuelan Virus Equine Encephalomyelitis in Trinidad, Bull. U. S. Army Med. Depart. 75: 96 (April) 1944.

York, in 1942 to Dr. Ludvig Hektoen of Chicago and last year to Dr. Elliott P. Joslin of Boston. This award is recognized as one of the most distinguished honors within the gift of the American Medical Association. Any Fellow of the Association may submit nominations, which should be sent, together with a record of the scientific services of the nominees, to the chairman of the Committee on Distinguished Service Award, Dr. A. A. Walker, 2250 Highland Avenue, Birmingham, Ala., or to the Secretary of the Association at 535 North Dearborn Street, Chicago. Of all nominations received by the committee, five are submitted to the Board of Trustees of the Association, from which the Board selects three to be submitted to the House of Delegates at its first meeting at the time of the annual session. Immediately on submission of the nominations by the Board of Trustees, the House of Delegates by official vote selects the recipient of the honor, to whom the Distinguished Service Medal is presented at the meeting at which the President-Elect is installed as President, which is usually on Tuesday evening of the week of an annual session. An extended list of distinguished physicians nominated for this award will enable the committee, the Board of Trustees and the House of Delegates, all of whom participate in the selection, to determine for 1944 a recipient of distinction, whose nomination will reflect favorably on himself and the Association.

TRANSPORTATION TO THE ANNUAL SESSION

According to current rules of the Office of Defense Transportation, reservations for pullman space of the railroads cannot be made more than thirty days in advance. The time of the annual session is June 12 to 16. Many physicians will be coming to Chicago for various smaller meetings that occur on June 10 and 11; others will be planning to return home at various times during the meeting. Therefore this comment is published to warn physicians well in advance of the necessity for making reservations for transportation at the earliest possible moment in relation to the trip. The entire trip should be planned so that reservations may be secured for coming to Chicago and returning home. This may require two trips to the reservations office—one for the trip going and the other for the trip returning. Transportation out of Chicago is under great pressure even in ordinary times. It will not be wise for a doctor to wait to purchase his return transportation until after his arrival in Chicago.

"THE STORY OF DR. WASSELL"

Next week the city of Little Rock, Ark., will be the site of a première of an unusual picture called "The Story of Dr. Wassell," directed by Cecil B. DeMille and produced by Paramount. The picture portrays the career of Dr. Corydon M. Wassell of Little Rock, somewhat romanticized, but follows nevertheless the high points of his life. Thus it includes his practice in Arkansas, his service as a medical missionary with a feeling for research, and his great accomplishment in transporting a group of wounded sailors across Java while the Japs were invading the island. Probably the most dramatic single incident in the picture is the introduction of the voice of the President of the United States when in his fireside chat on April 28, 1942 he quoted the official Navy report regarding Dr. Wassell and described the accomplishment for which he received the Navy Cross and the Officer's Cross in the Order of Orange Nausau from Queen Wilhelmina of Holland. This picture should be an inspiration to every physician who, in the midst of his busy life these days, gets an opportunity to see it. It should, of course, do much to carry to the American people the great service that American physicians are rendering in the war.

BORIC ACID CAUSES MORE INFANT DEATHS

Boric acid accidentally administered in milk formulas given to infants has caused the deaths of 4 infants and affected 20 others, some of whom may also die, according to recent press reports. This occurred in a New London, Conn., hospital. Boric acid crystals, according to the reports, were incorporated in the milk formulas by mistake because of their similarity in physical appearance to dextrose crystals. Unfortunately this is not the first time that boric acid has been responsible for accidental infant deaths in a hospital. In 1927, through a confusion of technic, infants in the nursery of a Chicago hospital were given boric acid solution instead of drinking water, and 6 of them died. Although these accidents and a few others like them have occurred only rarely and have been widely separated geographically and by time, the need for more careful protective devices is apparent. Boric acid, although it has only minor toxic properties as compared with other substances, is extensively used in the care of the skin and eyes of infants, so that it must be strictly segregated from those substances which may be incorporated into infant foods.

AID TO DIAGNOSIS OF MENINGOCOCCIC INFECTIONS

The early accurate diagnosis of meningococcic infections has assumed more than ordinary importance in view of the congestion of populations in industrial and military areas. Recently, Bernhard and Jordan [1] found meningococci in smears from purpuric lesions in 27 of 40 cases of meningococcic infections with such lesions. On culture the organisms were isolated in 35 of these 40 cases. In 25 cases of meningitis which showed clear spinal fluid with normal chemical constituents, positive spinal fluid cultures were obtained. The authors conclude from this high proportion of positive results of smears and cultures from the purpuric lesions that this method is a highly satisfactory procedure for the rapid and early diagnosis of meningococcic infections. This may prove a particularly valuable aid to diagnosis in certain types of clinical cases, especially those without early manifest signs of meningeal involvement.

1. Bernhard, W. G., and Jordan, A. C.: Purpuric Lesions in Meningococcic Infections, J. Lab. & Clin. Med. **29**: 273 (March) 1944.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on War Participation of the American Medical Association, announcements by the Surgeons General of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war, and such other information and announcements as will be useful to the medical profession.

NUTRITIONAL ASPECTS OF CONVALESCENT CARE

It may be assumed that the soldier or sailor who has subsisted on normal service rations is in an excellent nutritional state up to the time he becomes disabled by illness or disease. Exceptions must be made of men who, because they were isolated when they incurred their disability, had not received full rations.

As soon as injury or disease occurs, malnutrition almost always begins. This is the result of two processes: first "toxic destruction of protein"—i. e., the direct effect of disease or injury in promoting destruction of tissues—and, second, diminished intake of food, because of inability or disinclination to eat. Both of these processes bear some relation to the severity of the injury or disease.

Although some wastage of tissue can be tolerated and has no easily demonstrable effect on strength and efficiency, the extent of such "harmless" deficiency is ill defined. There is ample evidence that any considerable nutritional deficiency is distinctly harmful: It first reduces tolerance for exceptional exertion; in its most severe form it is altogether incapacitating. Even a mild degree of malnutrition should, therefore, be prevented because, though its evil effect may be undetectable, it marks a step toward incapacity and each step makes physical efficiency more precarious.

The "toxic destruction of protein" can be alleviated only by effective treatment of the disease or injury from which it originates. Its evil effects are, however, exaggerated by inadequate dietary intake. Wasting from this cause can be prevented in a large proportion of patients, and even "toxic destruction of protein" may be reduced by the effective administration of fluid and food in proper quantities and proportions. In addition, by improving the general state of health these measures promote and shorten the processes of repair.

Attention is likely to be given to the dietary needs of persons who are suffering from serious diseases and injuries, although the regimen may not always be wisely directed. From a military standpoint more man-days could be gained by accelerating the recovery of those with less grave conditions who may be rapidly returned to active service. Every effort should be made, therefore, to prevent malnutrition and minimize wasting in acute or minor casualties as well as in men with more serious disabilities.

The average medical officer is so preoccupied with the specific treatment of the disease or injury which confronts him that he is prone to overlook details of dietary management, especially when there are no urgent indications. In addition, even if he has the best will in the world, he may be insufficiently acquainted with fundamental principles of nutrition. For both these reasons it would be well in hospitals with a sufficiently large staff to place the responsibility for general supervision of dietary management and nutrition of patients on a particular member or members of the medical staff of the hospital. These nutritional medical officers should not order diets for all the patients in the hospitals, but they should rather act as instructors and consultants to the medical officers in charge of wards and should see that good dietary principles are observed throughout the hospital.

Outlined in succeeding paragraphs are the general principles underlying nutrition, knowledge of which may be expected to enable the medical officer to mitigate wasting and to accelerate recovery of patients.

Emphasis should be placed on the importance of prevention rather than correction of nutritional deficits. The proverb "An ounce of prevention is worth a pound of cure" is nowhere more applicable than in the field of nutrition. By focusing his attention on the diets at the very onset of illness, the medical officer can avoid the necessity of treating the serious effects of prolonged malnutrition.

GENERAL PRINCIPLES

Obvious but often overlooked is the fact that food offered to a patient is of no value unless it is eaten. The amount of food actually consumed should be ascertained. If food offered to the patient is not eaten, the reasons must be learned and, if possible, corrected. Anorexia must be regarded as a challenge, not as an inevitable and irremediable consequence of disability. Although patients should be encouraged to eat as varied a diet as possible, idiosyncrasies cannot be altogether neglected. Failure to eat may arise from physical weakness, exhaustion or the fact that the necessary motions are painful. It may be necessary to feed patients under these conditions. Fluid or semisolid diets may be essential for seriously ill patients. In the absence of gastrointestinal disturbances patients who will drink freely can usually be given adequate protein and calories in the form of fluids if advantage is taken of the sense of thirst. This sense should not be too much dulled by water and nonnutrient fluids; nutrient fluids should be made available to quench it. Thirst may be stimulated by the intelligent use of salt (see next section). But fluid or semisolid diets, because they are not conducive to appetite, should not be continued if the patient is able to take solid food. The chief reason for giving fluids, semisolids and soft foods to the sick is to relieve them of the work of cutting or masticating the foods. All foods become liquid in the gastrointestinal tract except milk, which first coagulates in the stomach. In some conditions frequent feedings are desirable; in this case the total diet is best divided equally into the required number of meals. Intermediate feedings (between meals of a regular dietary) may only spoil the appetite for the regular meals. Night feedings, shortly before sleep, are usually well tolerated; high calory feedings, instead of the usual light fluids, may be given to advantage at this time.

After a conference on Nov. 16, 1943, the Committee on Convalescence and Rehabilitation requested Dr. J. P. Peters, Yale University, and Dr. Robert Elman, Washington University, to draw up a report embodying methods of treatment which will maintain the best possible nutritional state in patients who are sick or injured. This request was made because of the belief that the use of well established principles of nutrition may diminish the catabolic effects of illness and therefore shorten the duration of convalescence. This report was presented at a meeting on Dec. 17, 1943 and was then modified by the authors and the committee to its present form. Acknowledgment is made of the contribution of the following men to the discussions which led to this report: Drs. Fuller Albright, R. C. Darling and Allan Butler, Harvard University; Co Tui, New York University; L. E. Holt Jr. and J. E. Howard, Johns Hopkins; Ancel Keys, Minnesota; R. F. Loeb, Columbia; S. C. Madden, Rochester; W. C. Stadie, Pennsylvania.

It is also obvious that whenever possible the patient should eat his necessary food in the normal way. It is not only unnatural but laborious for the doctor and distressing to the patient to meet all dietary requirements by means of other devices. Tube feedings or parenteral injections should not be employed merely as a means of evading the difficulties which arise from simple anorexia. On the other hand, these two methods are preferable to malnutrition and should be used when indicated. Their use, indeed, should make it possible to avoid malnutrition even if the patient is unable to take any food or fluid by mouth.

DIETARY ESSENTIALS

Water.—Enough water must be given to provide for insensible and sensible perspiration and for the production of sufficient urine to enable the patient to excrete the waste products that must be eliminated, without depleting the essential water stores of the body. Loss of water by the skin varies with the environmental temperature and the total caloric expenditure. The best criteria of an adequate water supply are:

(*a*) The volume of urine, which should not fall below 1,000 cc. in febrile patients; (*b*) the specific gravity of the twenty-four hour urine, which should not exceed 1.020, and (*c*) normal elasticity of the skin and subcutaneous tissues, the moist appearance of the tongue and the absence of uncomfortable subjective sensations of thirst.

Forcing fluids—i. e., inducing a patient to take uncomfortably large quantities of plain water—is seldom indicated. It is tiring and distressing to the patient and often impairs appetite. If a large intake is necessary, enough salt should be given to promote thirst.

Salt.—Animals derive their sodium salts almost entirely from sodium chloride added to their food. If the sodium salts of the body become depleted, water is not properly retained and dehydration results. In addition, sodium deficiency promotes circulatory failure. Patients with sodium depletion lose thirst, appetite and strength. If the sodium deficit becomes great, circulatory collapse may supervene.

Normal kidneys conserve sodium and chloride most efficiently. Chloride practically disappears from the urine as soon as its concentration in the serum falls appreciably below normal. If the urine contains little or no chloride (that is, yields little precipitate when treated with silver nitrate), it may be presumed that there is a salt deficiency. An exception must be made of patients with gross renal insufficiency, lobar pneumonia, advanced chronic tuberculosis and other destructive pulmonary diseases. In these conditions the kidneys do not retain their normal capacity to conserve salt. Consequently, urinary chloride excretion may continue after serum chloride has fallen below normal limits.

The insensible perspiration (fluid lost through the lungs and by the skin without sweating) amounts to 1,000 to 1,500 cc. and contains no salt. Sweat and exudates do contain salt that must be replaced. The stomach has no regard for the salt which does not cease even when serum sodium and chloride are depleted. Administration of water (ice in water) by mouth in the face of persistent vomiting only washes salt from the body and enhances dehydration, as does continuous gastric suction and lavage. For lavages of all kinds, isotonic solution of sodium chloride, not water, should be used.

All persons, unless they have congestive heart failure or nephritis with edema, should receive at least 5 Gm. of sodium chloride daily. The average normal diet contains more than this. If, however, patients do not eat enough of their diets or subsist chiefly or entirely on simple fluids, containing only carbohydrate, extra salt should be given. This may be introduced in broth or tomato juice or even in milk and fruit juices. Administration of adequate amounts of salt will often increase the intake of both food and fluid by creating appetite and thirst. Salt-depleted patients will not eat or drink well.

Protein.—Protein is indispensable; it cannot be replaced by any other food. A normal subject, starving, loses about 1 Gm. of tissue protein per kilogram of body weight per day. This deficit can be reduced to 0.3 to 0.5 Gm. by the administration of high calories in the form of carbohydrate and fat; it cannot be prevented entirely. Moderate amounts of carbohydrate alone will reduce protein loss considerably. In acute febrile diseases and after serious injuries protein wastage may rise to 3 or more grams per kilograms of body weight per day. This can be reduced only slightly by feeding carbohydrate. There is evidence that the lost tissue protein can be partly or wholly replaced and consequently that wasting can be mitigated or prevented by the administration of large amounts of protein and sufficient amounts of carbohydrate and fat to provide for the caloric requirements of the patient. This is a matter of great importance, since loss of tissue protein sacrifices the substance of liver and other important organs. It also results in depletion of serum proteins (hypoproteinemia), which ultimately leads to nutritional edema.

Every effort should be made to prevent this loss by administration of diets containing adequate amounts of protein of high biologic value containing all the essential amino acids in proper proportion. For this purpose, milk and eggs (the latter preferably cooked) may be used if patients are unable to take solids. Ground meats may, however, be given earlier and more freely than is generally believed.

Diets for sick or injured persons should contain 100 Gm. or more of protein daily. Nothing less than 1 Gm. of protein per kilogram of body weight per day can be regarded as a safe subsistence ration for a normal adult.

Carbohydrate.—A small amount of carbohydrate, perhaps 100 Gm. per day, is required to prevent ketosis in man. If this is not given, protein is broken down to provide carbohydrate. Granted sufficient protein and this minimum of carbohydrate, well nourished subjects can derive most of the additional calories needed from body fat, without serious injury.

Fat.—The least important element of the diet in acute disease is fat. Indeed, fat comprises the only large store of calories on which the body may draw without depleting essential tissues. In prolonged wasting conditions, however, fat deposits may become exhausted. It is, therefore, advisable if possible to prevent excessive loss of fat by giving high calories. For this purpose fat itself is peculiarly suited because it provides the greatest number of calories in the smallest bulk. The digestive system of most ill or injured persons tolerates, digests and absorbs fat well if it is given in palatable form with suitable carbohydrate vehicles. Nevertheless, if there is a limitation of the amount of food a patient can take, it is far better to give precedence to protein.

Vitamins.—Starving animals appear to acquire at first no vitamin deficiencies because for short periods they derive adequate vitamins in suitable proportions from their tissues. However, vitamin deficiencies develop after considerable periods on inadequate diets. The utilization or excretion of certain vitamins may be specifically increased by particular diseases, especially those which accelerate metabolism. Nothing is as effective in preventing vitamin deficiencies as a generous mixed diet. Complete oral mixtures of vitamins, especially brewers' yeast and other satisfactory preparations of vitamin B elements, when given in adequate quantities may destroy the appetite for food. They should therefore be used with caution as supplements to diets. Although complete vitamin mixtures for parenteral injection are not available, some important vitamins may be given readily.

Although a full well balanced diet best meets nutritional needs, it is frequently impossible for the injured or sick to take such a diet. It then becomes necessary to give priority to the food elements which are most urgently needed. The accompanying table lists in order of importance the various dietary constituents and the amounts of each which are required.

In patients previously well nourished, suffering from a disability or illness of short duration no serious harm develops from failure to maintain a high calory or fat intake, since the necessary calories will be derived from body fat if the minimum requirements for water, salt, protein and carbohydrate are met. When the patient is undernourished and the illness is long drawn out, fat stores may be depleted. The maintenance of adequate caloric intake then changes from a merely desirable part of therapy to a matter of more urgent importance.

If a patient had ample stores of vitamins before becoming sick, special efforts to supply these essential elements are not necessary during most acute illnesses. If the patient had been previously depleted of vitamins or is unable for a long period to take a balanced diet, vitamins should be administered.

TUBE FEEDING

Feeding by stomach tube is not a satisfactory procedure. Insertion of the tube is time consuming for the physician and often not pleasant for the patient. In unconscious patients the possibility of aspiration of injected material into the lungs introduces an element of danger.

In general, tube feeding should not be used until an honest effort has been made to have the patient eat. Such effort includes provision of palatable food of a type most appealing to the patient and some personal attention by the physician to overcoming the patient's distaste for food. When gavage is used, it should always be done as a temporary expedient with the patient's full knowledge that it will be discontinued as soon as he eats an adequate amount. However, there are

Dietary Constituents and Amounts Required

	Minimum Need	Average Requirements in Sick Patient
1. Water	2,000 cc.	3,000 cc.
2. Salt	5 Gm.	10 Gm.
3. Protein	75 Gm.	100-150 Gm.
4. Carbohydrate	100 Gm.	100-300 Gm.
5. Fat	(See discussion)	(See discussion)
6. Vitamins	(See discussion)	(See discussion)
7. Calories	(See discussion)	(See discussion)

clinical situations in which tube feeding is the only practicable means of preventing serious malnutrition of the patient. It may be necessary to resort to this procedure when the amount of nursing and other ward assistance is limited so that personnel is not available to spoon feed patients who are unable to feed themselves. In most instances the nasal route should be used for insertion of a moderate-sized tube, and the tube should be allowed to remain in place, with regular feedings administered at two to four hour intervals.

The material inserted through a feeding tube should always be warmed to body temperature. Large volumes and rapid rates of injection should be avoided. The material should be concentrated and should contain the necessary amounts of salt and protein, as well as carbohydrate and fat, for the provision of caloric needs, as for any well balanced diet. Casein hydrolysates in powdered form can be used to provide an adequate nitrogen intake, especially when there is evidence (diarrhea) that whole protein is inadequately digested. Hydrolyzed protein can often be assimilated by sick patients in much larger amounts than whole protein.

PARENTERAL FEEDING

Parenteral injections are to be looked on as temporary substitutes for normal eating, should never be used in the absence of specific indications and should never be regarded with complacency. However, all physicians are familiar with the great benefits which have accrued from the availability of methods for the parenteral administration of water and salt to patients unable to take these essential substances by mouth. Under many circumstances the provision of other nutrient materials parenterally has as great importance for the welfare of the patient as does the parenteral administration of fluid.

Parenteral feedings should be planned always with the view of introducing, in the smallest practicable volume of fluid and in the shortest time, the quantities and proportions of materials required to meet the needs of the recipient as they have been outlined. Administration of excessive amounts of fluid over unnecessarily long periods distresses and exhausts patients and wastes material and the time of attendants.

Water.—Water is the vehicle for all parenteral nutrient materials. At times, however, it may be necessary to give some water in addition to the amounts required for solvent purposes. In this case, since pure water cannot be injected, dextrose solution must be used. The dextrose is burned, providing calories, while the water is left in the body. The proportions of sugar and water may be varied in accordance with the needs for these two constituents.

Enough water should be given to replace water lost by insensible and sensible perspiration, vomiting, diarrhea and exudation and, in addition, sufficient to provide 1,000 cc. of urine (1,500 cc. if there is high fever and reason to suspect excessive toxic destruction of protein). It is impossible to state with accuracy the exact amount needed because of the wide variation under different clinical conditions. However, when a patient is unable to take any fluid by mouth, his minimum requirements will rarely be less than 2,000 cc. per day and will usually be 3,000 cc. or more.

Salt.—The salt requirements of an individual can be adequately supplied over moderate periods by the injection of an adequate volume of isotonic solution of sodium chloride. The ratio of chloride to sodium is higher in such solutions than it is in body fluids, but, if enough is given to produce an adequate volume of urine, the kidneys will excrete the excess chloride, while retaining sodium to form the necessary bicarbonate. Sufficient potassium, magnesium, calcium and phosphate will be obtained from destruction of tissues.

A minimum of 5 Gm. of sodium chloride a day should be given to all patients. Febrile subjects or persons who sweat excessively should receive additional amounts. In case of vomiting, enough should be given to replace salt lost in the vomitus. For subjects receiving water by mouth vomitus may be estimated to contain the equivalent of about 5 Gm. of sodium chloride per liter. For subjects receiving no water by mouth, fluid lost by vomiting should be replaced by an equal volume of saline solution. If the patient has become dehydrated by vomiting before treatment is instituted, enough saline should be given at the onset of therapy to repair the deficit; this may require as much as 5 to 10 liters of salt solution.

In addition to the saline solution, sufficient water should always be given in the form of dextrose solution to provide for the insensible perspiration, which contains no salt. This amounts usually to from 1,000 to 1,500 cc. daily, depending on the size and metabolism of the subject.

Dextrose.—A certain amount of carbohydrate is required to prevent ketosis and to mitigate nitrogen loss. Dextrose solution also permits the administration of approximate amounts of water without salt. As little as 100 Gm. of dextrose a day will prevent the gross ketonuria of starvation (i. e., excretion of enough ketones to yield positive nitroprusside tests in the urine) but will not prevent rise of ketone bodies in the blood. It is better to give dextrose in two doses than one, in order to insure continuous utilization. To provide enough calories to minimize protein wastage more than 100 Gm. daily is required.

Only 5 per cent dextrose solution should be used subcutaneously. Concentrations from 5 to 50 per cent may be injected intravenously. It is generally held that solutions stronger than 10 per cent should be used only in small quantities in conditions of emergency, because such solutions are likely to cause venous thrombosis. Concentrations as great as 15 per cent may, however, be used if they are introduced slowly enough and if there is a free flow of blood around

the needle in the vein into which they are injected. A free flow of blood and slow introduction of fluid dilutes the solution at the point of injection to an innocuous concentration.

Dextrose can be added to solutions of salt and to protein hydrolysate without consideration of its osmotic contribution, provided it is injected so slowly that the dextrose is utilized as rapidly as it enters the body.

Protein.—Protein may be given as transfusions of whole blood, plasma, hydrolyzed protein or mixtures of amino acids.

Transfusions of whole blood and infusion of normal or concentrated plasma are not ordinarily thought of as nutritional measures. They are used for maintaining blood volume and circulation. Every hundred cubic centimeters of normal blood contains about 15 Gm. of hemoglobin and 4 Gm. of plasma protein. Hemoglobin is not suitable for replacement of tissue protein. However, injected plasma protein is metabolized to some extent, and so provides a source of nitrogen nourishment and protects, in part at least, against tissue wastage.

Solutions of hydrolysates of casein or other high grade proteins have recently been employed and represent a more physiologic method of providing nitrogenous food parenterally, because food protein is normally hydrolyzed before absorption. Of the various hydrolysates available only one has been demonstrated to be safe, well utilized and capable of maintaining nitrogen equilibrium in man. This hydrolysate is prepared from casein by digestion with pancreatic enzymes.[1] Acid hydrolysates should have certain theoretical advantages. Up to the present time it has been impossible to produce acid hydrolysates without destroying certain essential amino acids, notably tryptophan. Since means of circumventing this oxidation have been devised, satisfactory acid hydrolysates may become available. Mixtures of pure amino acids suitable for injection have definite advantages, but they are expensive and are not yet available in large quantity.

It has been demonstrated that the nitrogen requirements of animals and patients may be supplied for long periods by infusions of casein hydrolysate or pure amino acid mixtures. Like all other parenteral methods of feeding, however, this must be regarded as a temporary substitute for normal eating. It is a procedure, moreover, that requires careful attention to detail.

The casein hydrolysate is usually prepared in 5 per cent concentration dissolved in 5 per cent dextrose solution. When neutralized to a p_H of 6.5, a liter of this solution contains 5 Gm. of sodium chloride. A liter of such a solution contains the equivalent of 50 Gm. of protein. Between 1.5 and 2 liters per day are therefore required to meet the basic demands of a normal man for protein. If solutions of casein hydrolysate are properly prepared, they should provoke no pyrogenic reactions. If they are injected too rapidly (faster than 500 cc. of a 5 per cent solution per hour in an adult of normal size) nausea or vomiting may be induced.

Fat.—At present no preparation of fat suitable for intravenous injection is available. Such preparations are feasible and have been made and used in emulsions up to 30 Gm. of fat per hundred cubic centimeters. The fat emulsions would have great theoretical value in any situation in which maintenance of a high caloric intake by parenteral injection is indicated, since each hundred cubic centimeters of a 30 per cent fat emulsion would provide 270 calories.

Vitamins.—During short sicknesses vitamins are not required, especially if the patients are not extremely malnourished. However, there are available preparations of certain vitamins for parenteral use, which should be given to patients who cannot eat a balanced diet during the course of prolonged disability. The most important ones are listed, with the daily doses recommended: thiamine (B_1), 10 mg.; riboflavin (B_2), 5 mg.; nicotinic acid, 20 mg.; ascorbic acid (vitamin C), 100 mg.

1. In this report all mention of casein hydrolysate for intravenous use refers to this enzymatic hydrolysate, the product of a single manufacturer. It is probable that other preparations will be developed in the future and proved by adequate clinical trial to be equally safe and efficacious.

GENERAL DIRECTIONS FOR PARENTERAL FEEDING

It is best to plan in advance the quantities of water and other constituents that will be required for the day, the times at which they are to be given and the routes by which they are to be administered. The total amounts of each component should first be estimated, after which they are translated into terms of parenteral materials that are available. Efforts should be made to use no more water than the patient requires.

Only isotonic solutions should be given subcutaneously, that is, normal saline or 5 per cent dextrose. The intravenous route is to be preferred to the subcutaneous for dextrose solutions, since dextrose tends to abstract water from the tissues at first because it diffuses more slowly than salt does. Saline solutions should not be reinforced with dextrose for subcutaneous injection because this makes a hypertonic solution. Dextrose can be added as desired to intravenous solutions because it is consumed, leaving only water. The temporary osmotic effect it produces is negligible or may be advantageous. If it is impossible to prepare the solutions fresh according to prescription, the desired concentration of dextrose may be made up by the addition of the required amount of sterile 50 per cent dextrose from ampules.

Solutions no stronger than 10 per cent of dextrose can be administered at the rate of 9 cc., or about 150 drops, per minute. If 15 per cent dextrose solution is used, the rate should be reduced to 6 cc., or about 100 drops, per minute. As a further precaution against venous thrombosis, the smallest possible needle (22 to 26) with a short bevel should be used, and care should be taken that it is held in place in such a way that the blood flow in the vein around the needle is not obstructed.

Casein hydrolysate solutions can be made up in 10 per cent concentration, which can be diluted to 5 per cent with dextrose solutions. Solutions prepared from the powder have a p_H of about 5.0. They should be brought to a p_H of 6.5 by the addition of sodium hydroxide before use.

EXAMPLES

1. It is desired to provide a nonfebrile patient who is unable to eat or drink but is not vomiting nor sweating and who has no large, exposed exuding surface for one day with water, salt and enough dextrose to prevent gross ketosis:

Water	1,500 to 2,000 cc.
Salt	5 to 8 Gm.
Dextrose	100 Gm.

1,000 to 1,200 cc. of 10 per cent dextrose and 500 to 800 cc. of isotonic solution of sodium chloride will meet these requirements closely enough. The total amount selected should preferably be given in two equal instalments.

2. If there has been a large antecedent deficit of salt as a result of vomiting, sweating or transudation, the proportions of salt may be increased.

For example:

Water	3,000 cc.
Salt	27 Gm.
Dextrose	100 Gm.

In this case 100 Gm. of glucose or 200 cc. of 50 per cent dextrose is added to 3 liters of isotonic solution of sodium chloride and divided into two portions in the same manner.

3. To meet the requirements for the nutrition of a patient who will be unable to take any food or fluids for some days and therefore should receive a nutrient which will provide an adequate amount of some protein substitute:

Water	3,000 cc.
Casein hydrolysate	100 Gm.
Dextrose	300 Gm.
Salt	10 Gm.

This will require 2 liters of 5 per cent casein hydrolysate-5 per cent dextrose solution and 1 liter of 10 per cent dextrose solution, a total of 3,000 cc. Since the casein hydrolysate is neutralized, it will contain 5 Gm. of salt per liter, or 10 Gm. in 2 liters. Other convenient formulas can be devised by which the volume can be kept below 3,000 cc. The selected amount of solution should be injected over a period of about four hours or, preferably, in two equal instalments of two hours each. If the patient is given transfusions of whole blood or plasma, the amount of casein hydrolysate will be decreased.

MISCELLANEOUS

WARTIME GRADUATE MEDICAL MEETINGS

Additional subjects and speakers for Wartime Graduate Medical Meetings have just been announced:

At Station Hospital, Dow Field, Bangor, Maine: Acute Abdominal Emergencies, Dr. Edward H. Risley, May 16.

At Dispensary, U. S. Naval Air Station, Brunswick, Maine: The Pneumonias and Other Respiratory Infections, Dr. Alexander M. Burgess, May 18.

At Station Hospital, Fort Banks, Boston: Blood Dyscrasias and Transfusions, Dr. William B. Castle, May 18.

At Dispensary, U. S. Naval Construction Training Center, Davisville, R. I.: Cardiac Neuroses, Cardiac Emergencies and Cardiac Rehabilitation, Drs. Samuel A. Levine and T. Duckett Jones, May 18.

At Fort H. G. Wright, Fishers Island, New York: Stomach, Biliary Tract and Intestinal Disorders, Dr. John C. Leonard, May 18.

At Station Hospital, Bradley Field, Windsor Locks, Conn.: Acute Abdominal Emergencies, Dr. Thacher W. Worthen, May 18.

At Camp Kilmer, New Jersey: Rickettsia Infections, Dr. William Sawitz, May 8; Water and Solute Balance in Health and Disease, Dr. John Eiman, May 29.

At England General Hospital, Atlantic City, N. J.: Malaria, Dr. W. Harding Kneedler and Dr. William Sawitz, May 2; Leishmaniasis, Dr. Julia Morgan and Dr. William Sawitz, May 16.

At Fort Monmouth, New Jersey: Diagnosis and Treatment of the Neuropsychiatric Patient in a Naval Hospital, Comdr. T. N. Spessard, May 3; Head Injuries: Their Diagnosis and Treatment, Dr. Temple Fay, May 10; Relationship of Pain and Tenderness to Body Mechanics, Dr. John C. Howell, May 17; Treatment of Burns and the Closure of Surface Defects by Skin Grafts and Flaps, Dr. Hans May, May 24; Viral Pneumonia, Dr. Hobart Reimann, May 31.

At Indiantown Gap, Pa.: Head Injuries: Their Diagnosis and Treatment, Dr. Temple Fay, May 3; Acute Glomerulonephritis (Trench Nephritis), Dr. George Morris Piersol, May 10; Blood and Plasma Bank and the Use of Its By-Products, Lieut. Clifford K. Murray, May 17; Malignancy as Seen in the Armed Forces, Dr. Stanley Reimann, May 24; Limitations of Fluoroscopy, Dr. W. Edward Chamberlain, May 31.

At Philadelphia Naval Hospital: Management of Pneumonia, Dr. Harrison F. Flippin, May 12; Limitations of Fluoroscopy, Dr. W. Edward Chamberlain, May 26.

At the U. S. Naval Hospital and U. S. Naval Academy Dispensary, Annapolis, Md.: The Pneumonias and Other Respiratory Infections, Dr. Luther L. Terry, May 19.

At Camp Lee, Virginia: Rheumatism, Lieut. Joseph L. Hollander, May 5; Prevention and Treatment of Wound Infections with Sulfonamides, Lieut. Col. Okla W. Sicks, May 12; Traumatic Surgery of the Abdomen, Dr. Frank S. Johns, May 19; Modern Diagnosis and Treatment of Pulmonary Tuberculosis, Dr. A. Barklie Coulter, May 26.

At Langley Field, Virginia: Anesthesia—Selection and Contraindications, Capt. Allen Widome, May 2; Psychosomatic Medicine, Lieut. Sidney U. Wenger, May 9; Traumatic Arthritis, Lieut. Comdr. Judson D. Wilson, May 16; Rheumatism, Major Terence Lloyd Tyson, May 23; Traumatic Surgery of the Abdomen, Dr. Robert L. Payne, May 30.

At Newton D. Baker General Hospital, Martinsburg, W. Va.: Crushing Injuries of the Extremities, Dr. Floyd Shaffer, May 1; Physiotherapy in War Wounded, Lieut. Comdr. Harry Etter, May 8; Psychosomatic Medicine, Dr. Jacob H. Conn, May 15; Shock, Dr. C. Martin Rhode, May 22; Prevention and Treatment of Wound Infections with Sulfonamides, Dr. Warfield M. Firor, May 29.

At Fort Eustis, Virginia: Psychoneurosis Among the Armed Forces, Dr. Claude L. Neale, May 11; Anesthesia—Selection and Contraindication, Capt. James P. Curran, May 25.

At Norfolk Naval Hospital, Portsmouth, Va.: Psychosomatic Medicine, Capt. Charles A. Spangler, May 11; Drainage of the Pleura, with Particular Relation to Chest Injuries, Dr. I. A. Bigger, May 25.

U. S. MARITIME SERVICE HOSPITAL CORPSMAN TRAINING

Lieut. Fred Edwards, regional public relations officer of the U. S. Maritime Service, recently announced that, for the first time in the history of the United States Merchant Marine, trained medical persons are now sailing aboard the freighters and tankers of our merchant fleet. About two years ago War Shipping Administration officials foresaw that medical doctors would become too few to permit their assignment to sea duty aboard merchant ships. As a result of this prediction the U. S. Maritime Service hospital corpsman-assistant purser school was founded at the Sheepshead Bay training station, New York. Men who qualify are given five weeks "boot" training for their life at sea, then a twelve weeks course learning anatomy, physiology, hygiene and sanitation, first aid, emergency treatment, nursing, pharmacy and clinical laboratory. Since they have to double as pursers in the merchant marine, they next receive training to keep the ship's records. Then they graduate to assignment of four weeks duty in a marine hospital, where they proceed from department to department, applying their theoretical training. On completion of the twenty-seven weeks course the seagoing medical men are ready to "put to sea."

HOSPITALS NEEDING INTERNS AND RESIDENTS

The following hospitals have indicated to the Council on Medical Education and Hospitals that they have not completed their house staff quota allotted by the Procurement and Assignment Service:

(Continuation of list in THE JOURNAL, April 15, page 1140)

MASSACHUSETTS

Malden Hospital, Malden. Capacity, 271; admissions, 5,299. Dr. D. M. Morrill, Director (assistant resident—June 1).

St. Luke's Hospital, New Bedford. Capacity, 339; admissions, 6,144. Mr. Scott Whitcher, Superintendent (interns—October 1).

NEW YORK

Beth David Hospital, New York City. Capacity, 187; admissions, 3,985. Mr. Harold M. Salkind, Executive Director (interns).

Bronx Hospital, New York City. Capacity, 389; admissions, 8,075. Mr. William B. Seltzer, Superintendent (four interns—October 1; assistant residents, surgery—June 1, October 1).

NORTH CAROLINA

Watts Hospital, Durham. Capacity, 225; admissions, 7,475. Mr. Sample B. Forbus, Superintendent (surgical resident).

PENNSYLVANIA

Women's Homoeopathic Hospital, Philadelphia. Capacity, 200; admissions, 2,790. Miss Mary A. Smith, Administrator (assistant resident).

TENNESSEE

Nashville General Hospital, Nashville. Capacity, 305; admissions, 6,138. Mr. T. F. Connally, Administrator (2 interns, residents, medicine, obstetrics-gynecology).

WASHINGTON

Western State Hospital, Fort Steilacoom. Capacity, 3,005; admissions, 889 Dr. W. N. Keller, Superintendent (resident, psychiatry).

WEST VIRGINIA

Kanawha Valley Hospital, Charleston. Capacity, 165; admissions, 4,414. Dr. G. B. Capito, Director (intern—July 1).

COMMUNITIES IN NEED OF PHYSICIANS

In addition to the four communities mentioned in THE JOURNAL April 8, page 1068, the United States Public Health Service has announced that the following communities have applied for federal assistance in obtaining the services of physicians under the recently enacted law authorizing an appropriation of $200,000 for the relocation of physicians:

Summerville (Green County) Kentucky.
Prentiss (Jefferson Davis County), Miss.
Glenrock (Converse County) Wyoming.

Physicians interested in locating in these communities should communicate with the Surgeon General, United States Public Health Service, Washington (Bethesda Station), D. C.

ORGANIZATION SECTION

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—The President has transmitted to Congress a draft of proposed changes in the program for supplying obstetric and pediatric care to the wives and infants of servicemen, as follows: (1) Extension of the program is recommended to include the wives and infants of army aviation cadets; (2) it is proposed that not more than 4 per cent of the federal appropriation may be allotted to the states for administrative expenses on the basis of need as determined by the chief of the Children's Bureau; (3) it is proposed that the amount of federal funds to be appropriated for the continuation of the program shall be immediately available rather than available for expenditure during the fiscal year beginning July 1. H. R. 4519 has been reported to the House, authorizing an appropriation of $1,000,000 to enable the Administrator of Veterans' Affairs to furnish seeing eye dogs for blind veterans. H. R. 4559 has passed the House, making appropriations for the Navy Department for the fiscal year ending June 30, 1945. This bill continues the provision in existing law authorizing the use of appropriations for the Naval Establishment for the pay of commissioned medical officers who are graduates of reputable schools of osteopathy.

Bills Introduced.—S. 1820, introduced by Senator Russell, Georgia, proposes a federal appropriation of $65,000,000 for the fiscal year ending June 30, 1945 and for each fiscal year thereafter such sum as may be necessary but not in excess of $100,000,000 for any one fiscal year to enable the Secretary of Agriculture to provide federal assistance in the maintenance, expansion and operation of school lunch and milk programs. S. 1824, introduced by Senator Smith, South Carolina, and Senator Ellender, Louisiana, also proposes federal appropriations to establish and maintain school lunch programs to provide lunches and nutrition instruction incidental thereto for children while attending school. H. R. 4383, introduced by Representative Bennett, Michigan, proposes to extend the old age and survivors' insurance benefits of the Social Security Act to the employees of states, political subdivisions thereof and instrumentalities of states or political subdivisions, and to self-employed individuals. H. R. 4500, introduced by Representative Rogers, Massachusetts, proposes to insure the furnishing of necessary artificial limbs and other appliances to disabled World War II veterans and to provide for appropriate instruction and training in their use. H. R. 4560, introduced by Representative Gearhart, California, proposes an appropriation of $4,000,000 to construct a veterans' hospital and home of domiciliary care in central California, with a capacity of at least 1,000 beds, with necessary auxiliary structures, mechanical equipment, domiciliary and outpatient dispensary facilities, facilities for a diagnostic center and accommodations for all personnel. H. R. 4561, introduced by Representative Barry, New York, proposes an appropriation of $1,500,000 to construct a new veterans' hospital and diagnostic center in the county of Queens, city and state of New York. H. R. 4584, introduced by Representative May, Kentucky, proposes to remove the limitation on the right to command of officers of the Dental Corps of the Army which limits such officers to command in that corps.

WOMAN'S AUXILIARY

Arkansas

Mrs. Elizabeth Walferman, chairman of legislation in Arkansas, sent out two thousand folders to be distributed at auxiliary meetings, showing how the two billion dollars of taxes in the proposed Wagner bill would be used for political medicine.

A student loan fund is maintained for doctors in Arkansas. They have made seventy-one loans and report that all but eight have been repaid.

District of Columbia

Dr. Tibor Kereker spoke on "Current Topics" at the January meeting. Generous donations were made by the auxiliary to the "In Bed Club" of the Washington Heart Association and to the District of Columbia Tuberculosis Association.

Florida

At a recent meeting of the Duvall County auxiliary, held at the home of Mrs. Raymond H. King, an address entitled "Civilizations Disappear" was given by Mrs. Harold S. Cohn, editor of the Jacksonville *Journal*. At the March meeting Comdr. M. J. Capron of the United States Naval Hospital at Jacksonville spoke on "Penicillin."

Pennsylvania

Reports of the Berks, Cambria, Center, Crawford, Huntington, Jefferson, Lehigh, Lycoming, Mifflin and Philadelphia county auxiliaries were published in the *Pennsylvania Medical Journal*. All meetings were interesting and well attended, but a striking feature was the amount of charity done. Crawford County auxiliary made 240 garments for charity; Delaware collected books for the service men's library and gave gifts to the Medical Welfare Society and the Salvation Army; Lycoming County auxiliary purchased three war bonds and gave $15 to the Community Chest; Philadelphia auxiliary gave $500 to the Aid Association of the Philadelphia County Medical Association, $50 to the War Chest, $5 to the Baby Welfare and $100 to fill Christmas baskets for the needy. Also the members brought toys for the children in the Philadelphia General Hospital and made 142 nightingales for the same hospital.

OFFICIAL NOTES

DOCTORS AT WAR

Radio broadcasts of Doctors at War by the American Medical Association in cooperation with the National Broadcasting Company and the Medical Department of the United States Army and the United States Navy are on the air each Saturday at 4:30 p. m. Eastern war time (3:30 Central war time, 2:30 Mountain war time and 1:30 Pacific war time).

The titles and guest speakers for the next three programs are as follows:

April 22. "Men with Purple Hearts."
Speaker, Col. Augustus Thorndike, M. C., U. S. Army, Washington, D. C.

April 29. "Winds That Kill."
Speaker, Lieut. Edward L. Corey, U. S. N., Washington, D. C.

May 6. "They Shall Walk Again."
Speaker, Col. L. T. Peterson, M. C., U. S. Army, Washington, D. C.

Doctors at War will not be on the air May 13, having relinquished its time on that date to the Office of War Information for the broadcast of a nationwide program in connection with the Cadet Nurse Corps of the U. S. Public Health Service.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Advisory Board for New Medical College.—A physicians' advisory board for the new medical college of Alabama to be erected in Birmingham was appointed March 14 by Gov. Chauncey Sparks. Members are Drs. Wilbur M. Salter, Anniston, five year term; James S. McLester, Birmingham, four year term; William D. Partlow, Tuscaloosa, two year term, and Harry Lee Jackson, Birmingham, one year term.

Program on War Casualties for Civilian Physicians.—The professional staff of Northington General Hospital, Tuscaloosa, presented a program for the Tuscaloosa and Jefferson county medical societies March 20 to show the army's medical department's progress in the treatment of war casualties. Among the speakers were:

Lieut. Col. I. William Nachlas, M. C., Gun Shot Wounds.
Capt. Frederick T. Becker, M. C., Penicillin.
Lieut. Col. Thomas R. Wright, M. C., Pilonidal Cyst.
Lieut. Col. Nicholas Michael, M. C., Psychoneurosis.

John A. Andrew Clinical Meeting.—The John A. Andrew Clinical Society held a clinical session with the John A. Andrew Memorial Hospital at Tuskegee Institute, April 2-8. Among the speakers were:

Dr. Charles F. Sherwood, St. Louis, Plastic Repair of Weblike Scars.
Dr. Jacob Daley, New York, Typical Rhinoplasty.
Roscoe C. Brown, D.D.S., Specialist, U. S. Public Health Service, Address on Public Health.
Drs. Ulysses Grant Dailey and Leonidas H. Berry, Chicago, Medical and Surgical Management of Peptic Ulcer.
Dr. Wallace Byrd, Norfolk, Va., Syphilis as a Cause of Selective Service Rejection of Negro Youth.

There will be two symposiums, one on flight surgeon's activities, conducted by Lieut. Col. Richard C. Cumming, M. C., Major Harold E. Thornell, M. C., and Capt. Leroy R. Weeks, and one on mental hygiene conducted by Dr. Prince P. Barker, Tuskegee.

DISTRICT OF COLUMBIA

Meningitis Quarantine Ended.—The use of sulfonamide drugs recently made possible the waiving of the usual twenty-one day quarantine for persons exposed to meningitis. A three day quarantine of 300 women at Arlington Farms, Va., was in effect. Newspaper reports stated that four deaths had occurred in the outbreak. The first case was discovered in Louisiana Hall at Arlington Farms accommodating 334 women government workers. One woman died while being transferred from Arlington Farms to a hospital in Washington, a year old child died at Children's Hospital, Washington, one woman died in Suburban Hospital, Bethesda, Md., and another woman died in Freedmen's Hospital, Washington.

Physician Receives Spingarn Medal.—Dr. Charles R. Drew, assistant professor of surgery, Howard University College of Medicine, Washington, has been awarded the Spingarn Medal for 1943 for the highest and noblest achievement by an American Negro. The award, which was announced by the National Association for the Advancement of Colored People, went to Dr. Drew for his work while medical supervisor of a blood transiusion project sponsored jointly by the Blood Transfusion Association and the American Red Cross of New York. Dr. Drew, together with Dr. John Scudder, New York, was instrumental in developing technics for the mass collection of blood plasma and the preservation of plasma for shipment overseas. The work was carried on during the years 1938-1941.

ILLINOIS

Rocky Mountain Spotted Fever.—A 23 year old man was reported to be ill with Rocky Mountain spotted fever in Alton, March 23.

Chicago

Northwestern Alumni Luncheon.—Northwestern University medical alumni will convene at a luncheon in the Palmer House May 17. The luncheon will be a feature of the annual meeting of the Illinois State Medical Society.

Course in Neuromuscular Anomalies of the Eyes.—The twelfth semiannual postgraduate course in neuromuscular anomalies of the eyes at the Children's Memorial Hospital will be conducted May 7-12 by Dr. George P. Guibor. Additional information may be obtained from the secretary of the course, 707 Fullerton Avenue, Chicago 14.

The Gehrmann Lectures.—Dr. Harold S. Diehl, dean of the medical sciences, University of Minnesota Medical School, Minneapolis, will deliver the Gehrmann Lectures for 1943-1944 at the University of Illinois College of Medicine May 17-19. His first lecture will be devoted to the cause and epidemiology of the common cold and the second to its prevention and treatment. The third lecture will be entitled "Some Recent American Epidemics."

Relocating Service Men and War Workers.—A conference will be held at the Drake Hotel, April 28-29, devoted to "Reabsorbing and Relocating Service Men and War Workers," under the auspices of the Society for the Advancement of Management. Included among the speakers will be representatives of the various phases of industry and some of the topics for discussion are guiding the service man's return to industry, organizing for relocation, problems of retraining, and the value of the job. A dinner session will be addressed by F. H. Kirkpatrick, manager of personnel administration, Radio Corporation of America, Camden, N. J., on "The Human Factor in Industrial Reconversion." One luncheon session will be addressed by a returned service man on "What the Man at the Front Thinks About His Return to Industry." Another luncheon session will be addressed by Charles W. Beese, M.E., head of the department of general engineering, Purdue University, Lafayette, Ind., on "The Influence of the War Effort on Management Education."

LOUISIANA

State Medical Meeting.—The sixty-fifth annual meeting of the Louisiana State Medical Society will be held at the Roosevelt Hotel, New Orleans, April 24-26, under the presidency of Dr. Charles C. deGravelles, New Iberia. Among the speakers on the program will be:

Dr. Waldo L. Treuting, New Orleans, and Byron J. Olson, P. A. Surg., U. S. Public Health Service, Clinical and Epidemiologic Features of an Epidemic of Severe Pneumonitis in Southwestern Louisiana.
John A. Lane, Surgeon, U. S. Public Health Service, Rupture of Intervertebral Disk.
Dr. Edgar Burns, New Orleans, Prostatic Obstruction and Some of Its Common Complications.
Dr. F. Walter Carruthers, Little Rock, Ark., Management of Shaft Fractures of the Long Bones.
Dr. Robert A. Katz, New Orleans, Psychosomatic and Medical Aspects of Peptic Ulcer.

At the president's dinner Tuesday evening Dr. Felix J. Underwood, Jackson, Miss., will deliver the annual oration. A feature of the state meeting will be a centennial exhibit reviewing the history of the *New Orleans Medical and Surgical Journal*. The woman's auxiliary to the state association will also hold its annual meeting at the Roosevelt Hotel, April 24-25.

MARYLAND

State Medical Meeting.—The Medical and Chirurgical Faculty of the State of Maryland will hold its annual session in Osler Hall, Baltimore, April 25-26, under the presidency of Dr. Jacob W. Bird, Sandy Spring, who will deliver an address entitled "Do We Need Federal Medicine?" Among other speakers on the program will be:

Dr. William H. F. Warthen, Towson, A County Health Program in War Time.
Dr. Arthur M. Shipley, Baltimore, Report of the Committee on Medical Service and Public Relations Regarding the Wagner-Murray-Dingell Bill.
Dr. Harry Arthur Cantwell, North East, The Toxic Effects of TNT and the Care of Workers in a Munition Factory.
Dr. Dexter M. Bullard, Rockville, The Practitioner as a Psychiatrist.
Dr. Albert Austin Pearre, Frederick, Fever of Obscure Origin.
Dr. Perry F. Prather, Hagerstown, Evaluation of the Pneumococcus Antigen as Measured by Pneumonia Prophylaxis in Maryland.

Dr. Allen O. Whipple, Valentine Mott professor of surgery, Columbia University College of Physicians and Surgeons, New York, will deliver the Trimble Lecture on "Hyperinsulinism in Relation to Pancreatic Tumors." A round table luncheon will be conducted by Drs. James G. Arnold Jr. and Bartus T. Baggott, Baltimore, on neurosurgery and tuberculosis respectively.

MASSACHUSETTS

Administrative Appointment at Harvard.—Alfred Le Roy Johnson, D.M.D., professor of clinical dentistry at Harvard University, has been appointed administrative officer of the new School of Dental Medicine at Harvard and associate dean of the faculty of medicine. Dr. Johnson graduated at Tufts College Dental School in 1904. He has served as professor of orthodontics at Tufts College, University of Michigan, University of Pennsylvania and as research associate in experimental genetics at Cornell University Medical College, New York. He was named to his professorship at Harvard in 1942.

NEBRASKA

State Medical Meeting.—The Nebraska State Medical Association will hold its annual meeting at the Hotel Fontenelle, Omaha, May 1-4, under the presidency of Dr. Albert L. Cooper, Scottsbluff. Among the out of state speakers will be:

Dr. Hans C. S. Aron, Chicago, Some Clinical Implications of Recent Advances in the Knowledge of the Vitamins.
Dr. Oliver E. Van Alyea, Chicago, Modern Trends in Sinus Therapy.
Major Oliver R. McCoy, M. C., Public Health Importance of Tropical Diseases in Returned Soldiers.
Dr. Alfred W. Adson, Rochester, Minn., The Federal Challenge to the Practitioner of Medicine.
Dr. Clarence Dennis, Minneapolis, Surgical Treatment of Upper Abdominal Pain.
Dr. Will F. Lyon, Chicago, The Holding Power of Various Types of Screws in Bone.
Dr. Guy A. Caldwell, New Orleans, The Influence of Bacteriostatics and Anti-Biotics in the Treatment of Compound Fractures and Wounds.
Dr. Guy W. Leadbetter, Washington, D. C., The Problem of the Fractured Hip.
Dr. Willard R. Cooke, Galveston, Texas, A Study of Gonorrhea in Women.
Dr. Frederick H. Falls, Chicago, Abortion.

At an army session Lieut. Col. Nathan K. Jensen, M. C., will speak on "War Wounds of the Extremities," Lieut. Col. Edward B. Badger, M. C., "Medical Problems of Selective Service" and Lieut. Col. Edgar van Nuys Allen, M. C., will discuss "Functional Somatic Disorders in the Army" from the consideration of the internist and Lieut. Col. Clarke H. Barnacle, M. C., from the viewpoint of the psychiatrist.

NEW YORK

Personal.—Dr. Howard P. Carpenter has resigned as director of the laboratory of the Poughkeepsie board of health, effective May 1. Newspapers inucated that Dr. Carpenter would also resign as director of the laboratory of the Hudson River State Hospital and as deputy county medical examiner. He plans to go to Vermont, it was stated. Dr. Carpenter resigned as secretary of the Dutchess County Medical Society in 1941 after holding the position for twenty-seven years.—— Dr. Bruno Leichtentritt has been appointed medical director of the Irvington House, an institution for the care of children with rheumatic heart disease in Irvington. Dr. Leichtentritt had been for more than five years a fellow of the Children's Fund of Michigan at the William J. Seymour Hospital, Eloise, according to *Detroit Medical News.*

Research Professorship in Pediatrics.—Dr. Edward M. Bridge, associate in pediatrics, Johns Hopkins University School of Medicine, Baltimore, has been named to a new research professorship in pediatrics at the University of Buffalo School of Medicine and in charge of the Statler pediatrics research department in the Children's Hospital, Buffalo. A floor of the hospital is being remodeled to house the laboratories, which have been provided by a grant of the trustees of the late E. M. Statler. Dr. Bridge will conduct research in drugs used in the treatment of epilepsy, the water and sugar requirement of sick children, the care of premature infants and other pediatric problems. At the university he will encourage and promote research in the diseases of children and stimulate research among medical students. Other changes at the school include the appointment of Oliver P. Jones, Ph.D., assistant professor of anatomy, as head of the department of anatomy, succeeding Donald Duncan, Ph.D.

New York City

Phi Delta Epsilon Lecture.—Dr. Arthur M. Fishberg will deliver the annual Phi Delta Epsilon lecture at the Long Island College of Medicine, Brooklyn, April 27, on "Recent Advances in Hypertension."

Changes in Sanitary Code.—A recent amendment to the city sanitary code provides that in no case shall a person previously convicted of a prostitutional offense be released from detention in a hospital designated by the city department of health unless such a person is no longer infected with a venereal disease in a communicable form. An additional amendment includes meningococcus meningitis (epidemic cerebrospinal meningitis) and typhus fever on a list of causes of death requiring the body of the deceased to be immediately and permanently sealed in a casket before removal from the place of death. Another amendment stipulates that all forms of plague shall be considered reportable diseases.

Gift of Apothecary Shop to Columbia.—A fully equipped "apothecary's shop of the eighties," complete with prescription counter, ointment jugs, iron mortars and shelves of samples of the "patent medicine' era," was presented formally to Columbia University College of Pharmacy by Arthur J. Kinsman, trustee of the school. It was installed as a permanent teaching exhibit in the college. According to the New York *Times,* the prescription counter of the old store once stood in Roediger's Drugstore at 46 Market Street, which opened in the city in 1832. A wooden safe of the same age, which was purchased by the college of pharmacy in 1843, stands in a corner of the store. The *Times* states that the old "patent medicines," including "positive pain cure," gout remedies, magic oils, chill tonics and hair growers, are also included. A cordial for babies carries on its label "cure for colic and teething." A large porcelain jar with a perforated top is labeled "leeches" and was used to carry a ready stock of living cures for black eyes. In making the presentation to the college, Mr. Kinsman referred to the pharmaceutical products as reminders of the "patent medicine" era of the 1870's, "those glorious days of the wouldbe cure-alls, good for man or beast."

NORTH CAROLINA

Committees Named to Work with New Medical Care Commission.—On March 11 Governor Broughton announced the appointment of six subcommittees to work with the new North Carolina Hospital and Medical Care Commission. The committees are four year medical school for the University of North Carolina and hospital facilities, Dr. Paul P. McCain, Sanatorium, chairman; hospital and medical care for rural population, Thomas J. Pearsall, Rocky Mount, chairman; hospital and medical care for industrial and urban population, Charles A. Cannon, Concord, chairman; special needs of the Negro population, C. C. Spaulding, Durham, chairman; mental hygiene and hospitalization, Dr. James W. Vernon, Morganton, chairman, and hospital and medical care plans in other states, Dr. William M. Coppridge, Durham, chairman. The program of the newly appointed commission is designed to see that "no person in North Carolina shall lack adequate hospital care or medical treatment by reason of poverty or low income" (THE JOURNAL, March 25, p. 939).

State Medical Meeting.—The ninety-first annual session of the Medical Society of the State of North Carolina will be held at the Carolina Hotel, Pinehurst, May 1-3, under the presidency of Dr. James W. Vernon, Morganton. The preliminary program includes the following speakers:

Col. Burr N. Carter, M. C., The Recent Trends in the Care of the War Wounds.
Judge L. R. Varser, Lumberton, Socialized Medicine From a Layman's Point of View.
Dr. Clarence H. Smith, New York, Ménière's Symptom Complex.
Dr. James W. White, New York, Ocular Muscle Paralyses—Their Diagnosis and Treatment.
Dr. Louis K. Diamond, Boston, Transfusion Reaction Due to the Rh Blood Type.
Dr. Neka B. Hon, Bethesda, Md., Recent Experiences in the Intensive Treatment of Syphilis.
Dr. James E. Paullin, Atlanta, Ga., President of the American Medical Association, Medical Planning for the Postwar Period.

At the president's dinner, Strickland Gillilan, Washington, D. C., author of the poem "Off Agin, On Agin, Gone Agin, Finnigin," will be the guest speaker.

OHIO

Food Information Center.—The Cleveland Health Council, in cooperation with the Cleveland Health Museum, has established a food information center at the museum. A nutritionist is available at the museum one evening a week to answer questions on food and food problems.

State Medical Meeting in Columbus.—The ninety-eighth annual meeting of the Ohio State Medical Association will be held at Neil House, Columbus, May 2-4, under the presidency of Dr. Clifford C. Sherburne, Columbus. Among the speakers on the program will be:

Dr. Paul H. Holinger, Chicago, Cine-Bronchoscopy-Kodachrome Visualization of Endobronchial Pathology.
Dr. Oliver W. Hosterman, Columbus, Influenzal Meningitis.
Dr. Noel A. Gillespie, Madison, Wis., Factors that Influence the Success of an Anesthetic Administration.
Dr. Alexander A. Weech, Cincinnati, Hyperbilirubinemia in the Newborn.
Dr. Edward Harlan Wilson, Columbus, Treatment of Fractures as Related to Functional Recovery.
Anton J. Carlson, Ph.D., Chicago, Fatigue.
Melvin H. Knisley, Ph.D., Chicago, Motion Picture—Knowlesi Malaria in Rhesus Monkeys.
Dr. Edward L. Turner, Nashville, Tenn., The Dysenteries.

Special features of the meeting will include a discussion on functional and organic diseases of the gastrointestinal tract by Drs. Andrew C. Ivy, Chicago, and Arthur W. Allen, Boston, and special quiz discussion sessions on medicine, including tropical medicine, psychiatry and occupational diseases. At the annual dinner Wednesday evening Mr. Grove Patterson, editor, Toledo *Blade,* will give the principal address, on "Britain in Wartime." Other groups meeting during the annual session will include the woman's auxiliary to the state association, the Ohio Society of Anesthetists, the Ohio chapter of the American College of Chest Physicians and the Ohio State Radiological Society.

OKLAHOMA

Paul Fesler Appointed Temporary Executive Secretary.—Mr. Paul H. Fesler, formerly superintendent of the University Hospitals, Oklahoma City, and of the University Hospitals, Minneapolis, has been named on a temporary basis to act as executive secretary during the absence of Mr. Richard H. Graham, according to the state medical journal. Mr. Fesler was once superintendent of the Wesley Memorial Hospital, Chicago, and has served as president of the American Hospital Association.

Conference on Poliomyelitis.—At the suggestion of crippled children's agencies in Texas, Oklahoma and Kansas, three states seriously affected by the poliomyelitis epidemic of 1943, a conference on basic planning for dealing with such epidemics was held in cooperation with the U. S. Children's Bureau in Oklahoma City, February 23-24. Dr. Abram L. Van Horn, assistant director for crippled children, division of health services of the Children's Bureau, U. S. Department of Labor, was chairman of the conference.

VIRGINIA

Special Society Meeting.—The Virginia Society of Ophthalmology and Oto-Laryngology will be addressed at its twenty-fifth annual meeting in Lynchburg, April 29, among others, by Drs. John H. Dunnington, New York, on "Complications of Cataract Extraction" and Arthur T. Ward Jr., Baltimore, "Local Use of Sulfadiazine, Penicillin, Tyrothricin and Radon in the Field of Otolaryngology." Dr. Emmett T. Gatewood, Richmond, is president of the group and Dr. Meade C. Edmunds, Petersburg, is secretary.

The Stuart McGuire Lectures.—The fifteenth annual Stuart McGuire lectures were delivered at the Medical College of Virginia, Richmond, April 5-6. Dr. Winifred Overholser, superintendent, St. Elizabeths Hospital, Washington, D. C., spoke on "Modern Trend in Psychiatry" and Lieut. Col. William C. Menninger, chief of the army's division of neuropsychiatry, "Psychiatric Problems in the Army." The lectures were given in conjunction with a postgraduate clinic devoted this year to a series of psychiatric subjects.

WISCONSIN

Winners in Essay Contest.—The Milwaukee Academy of Medicine announces that first prize in the Horace Manchester Brown Memorial Essay Contest went to Dr. Robert H. Feldt, Milwaukee, for his paper entitled "Sulfanilamide as a Prophylactic Measure in Recurrent Rheumatic Fever: A Controlled Study Involving 131 'Patient-Seasons.'" Second prize went to Dr. Nathan M. Grossman, Milwaukee, for his paper on "The Left Auricle." The prizes were $100 and $50 respectively. The academy also announces that no award was made for the Rogers Memorial Essay Contest because, in the opinion of the judges, no papers were deemed worthy (THE JOURNAL, June 19, 1943, p. 553).

GENERAL

Examinations in Internal Medicine.—The American Board of Internal Medicine will hold oral examinations in Chicago, June 8-10. The closing date for the acceptance of applications is May 20. Communications should be addressed to the assistant secretary-treasurer of the board, Dr. William A. Werrell, 1301 University Avenue, Madison 5, Wis.

Association of Basic Science Boards Organized.—The American Association of Basic Science Boards was organized at a meeting in Chicago, February 15, with Orin E. Madison, Ph.D., Detroit, of the Michigan board, as president. Other officers include Charles D. Byrne, Ed.D., Oregon board, Eugene, vice president; Charles H. Carter, D.Sc., Iowa board, Fairfield, secretary-treasurer, and John S. Latta, Ph.D., Nebraska board, Omaha, and Rev. Nicholas H. Serror, O.P., Rhode Island board, Providence, executive committee.

Membership of Board of Neurological Surgery.—At a meeting of the American Board of Neurological Surgery in New York, March 26, it was voted unanimously that the number of members of the board nominated by the Society of Neurological Surgeons should be reduced from five to four and that the American Academy of Neurological Surgery should be invited to nominate one of their neurosurgical members to the board for a term of office, to begin in the summer of 1944.

Association of Cereal Chemists.—The thirtieth annual meeting of the American Association of Cereal Chemists will be held at the Nicollet Hotel, Minneapolis, May 23-26. A feature of the meeting will be a symposium on protein nutrition conducted by Richard J. Block, Ph.D., New York, "Evaluation of Food Proteins from the Essential Amino Acid Composition"; Herman J. Almquist, Ph.D., Berkeley, Calif., "Effective Use of Feed Proteins in Nutrition of the Chick," and Dr. Paul R. Cannon, Chicago, "The Nutritional Assay of Proteins by Means of the Adult Hypoproteinemic Rat."

Pan American Conference of National Directors of Health.—The fifth Pan American Conference of National Directors of Health will be held in Washington, April 22-29, to discuss wartime and postwar health programs. The subjects include air navigation quarantine, immigration, improved national and international disease reporting, aerial navigation, port sanitation, quarantine regulations and the adoption of an international health certificate. One feature of the meeting will be the preparation of a program for the XII Pan American Sanitary Conference, to be held in Caracas, Venezuela, in 1946. Health and hygiene authorities of the Latin American countries will be represented. Canada will also be represented.

Fund for Research in Psychosomatic Medicine.—The National Committee for Mental Hygiene announces the establishment of a fund for research in psychosomatic medicine to stimulate and subsidize research in the psychosomatic aspects of the diseases chiefly responsible for disability and death. The fund will be directed by Dr. Edward Weiss, Philadelphia, and administered under the direction of Dr. George S. Stevenson, New York, medical director of the National Committee for Mental Hygiene. Projects will be considered by a committee composed of Drs. Charles A. Aldrich, Rochester, Minn., Franz Alexander, Chicago, Stanley Cobb, Boston, John Romano, Cincinnati, and Lieut. Col. William C. Menninger. Additional information may be obtained from Dr. Weiss, 269 South 19th Street, Philadelphia 3.

Borden Prize Awarded to William Clark.—At the meeting of the American Chemical Society in Cleveland, April 5, the Borden Company Prize for 1944 of $1,000 for research in the chemistry of milk was presented to William Mansfield Clark, Ph.D., DeLamar professor of physiologic chemistry at the Johns Hopkins University School of Medicine, Baltimore, and chairman of the division of chemistry and chemical technology at the National Research Council, for his contributions to the application of acid-base theory to laboratory and plant practice. *Science* reports that, as a result of his work and writings, the old haphazard and often irrational procedures in the dairy industry and other industries have been fruitfully transformed during the past years to precise scientific manipulations.

Dr. Strode Succeeds Wilbur Sawyer at Rockefeller Foundation.—Dr. George K. Strode, associate director of the International Health Division of the Rockefeller Foundation in charge of the division's work in Europe, has been appointed director of the division to succeed Dr. Wilbur A. Sawyer, who will retire, effective September 1. Dr. Sawyer, who graduated at Harvard Medical School, Boston, in 1906, was appointed state director of the International Health Board in 1919. He has served as assistant regional director for the east, director of public health laboratory service, associate director of the International Health Division and, since 1935, director. Dr. Strode graduated at the University of Pennsylvania School of Medicine, Philadelphia, in 1912, receiving his master's degree in public health at Harvard in 1927. He has been a member of the International Health Division of the foundation since 1920, having been chosen a member for one year in 1916. He was assistant director for activities in Europe and the Near East from 1927 to 1938, when he became associate director. He was chairman of the Paris office from 1932 until 1938.

Nutrition Grants.—Grants totaling $131,000 for research projects in nutrition were approved by the board of trustees of the Nutrition Foundation at a meeting in New York, April 5. The grants are distributed among twenty-three colleges and universities in the United States and Canada and include renewal of grants for thirty-one research projects already in progress and three additional grants for studies at Harvard, Yale and Cornell. According to a release from the foundation, grants having greatest value thus far were "those dealing with army rations, human protein requirements, maternal and infant nutrition, dental caries and human vitamin requirements." The new grants authorized at the recent meeting include:

Harvard University, Cambridge, for training physicians in the human and public health aspects of nutrition.

Yale University, New Haven, Conn., in support of maternal and infant nutrition studies, based on carefully controlled nutrient intakes of primates (monkeys), other animals having been found not so satisfactory for the study of numerous human problems such as dental caries, physical deformities or functional impairment.

Cornell University, Ithaca, N. Y., for study of the biochemical mechanism of converting starches and sugar into fat.

Meeting of Bacteriologists.—The forty-fifth annual meeting of the Society of American Bacteriologists will be held at the Hotel Pennsylvania, New York, May 3-5, under the presidency of Ira L. Baldwin, Ph.D., Madison, Wis. Among the speakers will be:

Merton F. Utter, B.A.; Lester O. Krampitz, Ph.D., and Chester H. Werkman, Ph.D., Ames, Iowa, Oxidation of Acetyl Phosphate by Micrococcus Lysodeikticus.

Dr. Harold E. Pearson, Ann Arbor, Mich., The Distribution of Influenza Virus Type A in Infected Eggs and the Survival of Virus Under Certain Conditions of Storage.

Gordon C. Brown and Dr. Thomas Francis Jr., Ann Arbor, Mich., Embryonic Chick Antigens for Complement Fixation with the Viruses of Eastern and Western Equine Encephalomyelitis.

Maurice R. Hilleman, S.B., and Dr. Francis B. Gordon, Chicago, Immunological Studies on the Relationships of the Psittacosis-Lymphogranuloma Group of Viral Agents.

Reuben L. Kahn, Sc.D., and Elizabeth B. McDermott, Ann Arbor, The Verification Test in Postvaccination Cases.

Albert Milzer, Ph.D., Dr. Philip Lewin and Dr. Sidney O. Levinson, Chicago, Studies on the Influence of Fatigue, Chilling and Trauma on Experimental Poliomyelitis.

Selman A. Waksman, Ph.D., New Brunswick, Mode of Action of Antibiotic Substances.

Albert C. Hunter, Ph.D., Washington, D. C., Standardization of Assay of Penicillin.

Dr. William S. Tillett, New York, An Analysis of the Therapeutic Action of Penicillin Based on the Clinical Response of Patients and Correlated Laboratory Findings.

Elaine Updyke, M.S., and Martin Frobisher Jr., Sc.D., Baltimore, Group B Streptococci and Malignant Diphtheria.

There will be round table discussions on recollections of the early days of bacteriology in New York City, problems concerning anaerobic bacteria, taxonomy and primary atypical pneumonia.

LATIN AMERICA

Health Activities in Latin America.—*Cinchona.*—Studies to determine the practicability of developing new cinchona plantations in Mexico are being conducted by the department of health, according to the New York *Times*, April 9. About 60,000 cinchona plants are under cultivation in the state of Chiapas. Production of quinine eventually may be sufficient to meet all domestic requirements and provide an export surplus, it was stated. Important progress has been made in the cooperative hemispheric effort to cultivate quinine-yielding cinchona, according to William C. Davis of the staff of the United States Office of Foreign Agricultural Relation in the *Inter-American Economic News*. Quinine supplies for the United Nations are being obtained from Guatemala, Venezuela, Colombia, Ecuador, Peru and Bolivia, which countries, with Mexico, Costa Rica and Brazil, are cooperating with the United States to develop in the Western Hemisphere a sound cinchona industry. Colombia has contributed more bark from wild or native stands during the past year than any other country in this hemisphere. It was stated that in Colombia the bark from a related plant, botanically known as Remijia, contains enough quinine to make its harvest profitable under existing conditions. In Brazil cinchona production is still in the experimental stage. Small plantings have been made in the mountainous regions bordering the state of Minas Gerais, and cinchona seedlings supplied by the United States have been put out at Campinas and Baracea. The United States, through the department of agriculture and the foreign economic administration, is cooperating with all these cinchona producing countries. The foreign economic administration is concerned with the procurement of cinchona and such work as will expedite availability of high quality bark, and the department of agriculture is aiding through research, technical advice and demonstration in the growing of the plants. It is also sending quality seedling stock to the most promising production areas.

Physician Heads Identification Division.—Dr. Hubert Wallau, who is now in the United States studying traumatic surgery under the auspices of the Institute of Inter-American Affairs, an agency of the Office of Inter-American Affairs, is head of the identification division in Rio Grande do Sul, Brazil. Dr. Wallau is studying at the Boston City Hospital. In Brazil he is a member of the staff of the Santa Casa de Misericordia Hospital in Porto Alegre.

Society News.—Drs. Egidio S. Mazzei and Carlos Reussi were elected president and secretary, respectively, of the Society of Internal Medicine of Buenos Aires for 1944.——Dr. Ramón N. Ibarra Perez was chosen president and Dr. Guillermo Gonzalez Peris secretary of the Cuban Society of Dermatology and Syphilology for 1944.

New Publication.—The Argentine Psychoanalytic Association recently began the publication of its official organ, *Revista de psicoanalysis.*

Graduate Course in Legal Medicine.—A two year postgraduate course in legal medicine has been created by the Faculty of Medicine at the University of La Plata, Buenos Aires, Argentina, for physicians who wish to become specialists in this field. The course will be under the direction of Dr. José Belbey, professor of legal medicine of the Faculty of La Plata School of Medicine and adjunct professor of medicine in the School of Medicine of Buenos Aires, and includes lectures, seminars and actual clinical work. During the first year the curriculum includes legal medicine, clinical psychiatry, medicolegal toxicology, legal medicine and occupational diseases. The second year encompasses forensic psychiatry, criminology and principles of penal law, medicolegal necropsy and medicolegal aspects of workmen's compensation. Those completing the course will receive a specialist's diploma, according to the *Journal of Criminal Psychopathology.*

Hospitals for the Amazon.—Harold B. Gotaas of the Health and Sanitation Division, Office of Inter-American Affairs, has recently prepared a review on the hospital development program in Latin America entitled "Hospitals for the Amazon." The program, he points out, is being done as part of inter-American health and sanitation measures recommended by the Rio de Janeiro conference of American Foreign Ministers in January 1942, which measures have evolved into a continental program to improve health and sanitation conditions in areas important to the development of hemisphere resources and defenses. Nineteen of the American republics, including the United States, are participating. Mr. Gotaas, who is a sanitary engineer, discusses the project as it is carried out in the Amazon Basin, covering the territory of Brazil, Bolivia, Peru, Ecuador, Colombia and Venezuela. While this area has great tropical forests, wood is not suitable for the building materials, clay and brick being used instead, he says. New construction included a 20 bed hospital in Guayaramerin and in Pucallpa, Peru. In Iquitos a 100 bed hospital was one of the first projects in the Peruvian health program, which includes a 20 bed children's ward, 20 bed women's ward, 20 bed men's ward, a surgical section with operating and x-ray room, administrative wing with outpatient department, and kitchen and general service wing, water and sewerage facilities. At Santarem a 50 bed hospital, also of tile and brick construction, contains operating rooms, outpatient department and pharmacy. In addition many health centers and dispensaries are being erected.

New Monthly Epidemiologic Report.—With the March issue the *Monthly Report on Epidemiological and Vital Statistics* begins its regular appearance under the auspices of the Pan American Sanitary Bureau, Washington 6, D. C. The report replaces the tables on pestilential diseases which were published in the *Boletín* of the Pan American Sanitary Bureau. The purpose of the publication is to convey, in the quickest possible manner, to the national and international public health organizations, as well as to all other interested parties, the available information on the incidence and mortality of certain communicable diseases, as well as other biostatistical data on various countries, particularly those in the Western Hemisphere.

Personal.—Dr. George C. Dunham, executive vice president of the Institute of Inter-American Affairs, and assistant coordinator in charge of the basic economy department, Office of the Coordinator of Inter-American Affairs, has been promoted from brigadier general to major general, medical department, A. U. S., with rank from February 22. According to the *Newsletter*, Division of Health and Sanitation, of the coordinator's office, Clair E. Turner, Dr.P.H., of the professional training and health education section of the division recently spent time in Brazil, Peru and Chile to consult with respective field parties on health education programs.

FOREIGN

Typhus Epidemic Among Yemenite Refugees.—Professor I. J. Kligler, professor of bacteriology and hygiene, Hebrew University of Jerusalem, left with three Palestinian Jewish nurses for Aden by plane in February to organize medical relief for 1,600 Yemenite refugees, among whom a typhus epidemic has broken out. The mission was sent at the request of the Aden government, according to the *News Bulletin* published by the American Friends of the Hebrew University.

CORRECTION

Allergy to Lan-O-Kleen Soap.—In THE JOURNAL, Dec. 11, 1943, page 991, appeared an abstract of a workman's compensation case regarding an allergy to Lan-O-Kleen soap, which a workman was required to use in the course of his employment. The abstract of the case emphasized the fact that the employee had used the lava soap for six or seven years and did not develop an allergy until he adopted the Lan-O-Kleen soap. The concluding sentence of the next to last paragraph read "Lava soap was a poison to the workman, and his injury was compensable." In this sentence the words "lava soap" should have been "Lan-O-Kleen soap."

Foreign Letters

LONDON

(From Our Regular Correspondent)

March 18, 1944.

The National Health Service: Attitude of the British Medical Association

A mass meeting of the Metropolitan Counties Branch of the British Medical Association was held recently to hear an address by Dr. Charles Hill, secretary, on the White Paper, which he described as the government's first thoughts on the Beveridge scheme to provide a comprehensive medical service for all who wanted it, irrespective of income limit. Dr. Hill said he believed that the general reaction of the profession to the three "freedoms" set out in the paper was that they were worthy of full support, but the real test would be the extent to which these freedoms found expression in the administrative machinery and arrangements. They are: 1. Freedom for people to use or not to use the facilities; no compulsion for either patient or doctor; no interference in the making of private arrangements at private cost, if any one prefers to do so. 2. Freedom for people to choose their medical advisers. 3. Freedom for the doctor to pursue his professional methods in his own way. The personal doctor-patient relation was to be preserved and the whole service founded on the "family doctor" idea.

The proposal for a corporate body, Dr. Hill pointed out, was not accepted by the government. But whereas comprehensive service was preached in all other directions, he said, there was no comprehensive service planned for the center; rather the medical services would remain distributed among a multitude of government departments. An advisory body, the Central Services Council, was to be set up, consisting of both medical and lay members appointed by the minister, not specially elected for the purpose by the professional organizations. This, Dr. Hill thought, was wrong.

At the periphery, he continued, instead of the hoped for fundamental recasting of local government there was a compromise. There would be not fewer local authorities but more. The hospital services had to be dealt with regionally, but Dr. Hill thought it was regrettable that in creating the new type of body, the Joint Authority, the government had been unwilling to dilute the democratic principle by including, in the public interest, some nonelected professional and expert members.

On administration as a whole he said that the arrangements spit the profession into four groups: general practitioners in separate practice, general practitioners in health center practice, consultants appointed by voluntary hospitals and consultants appointed by local authorities. There was also a group whose position, Dr. Hill felt, must be viewed with considerable anxiety —their colleagues of the public health service. Dr. Hill also had misgivings as to the health centers. The Association had urged that these should be initiated for a period of experiment with a view to discovering the right type of group practice. This might be (1) the center with general practitioner beds, (2) the diagnostic center, concentrating on special methods of investigation and possibly treatment, (3) the true health center, in which both preventive and curative services are integrated or (4) the communal surgery. The last and least advanced of these types was adopted in the White Paper.

When practitioners participate in group practice health centers, remuneration is to be by salary or similar arrangement. The government needed to be converted on that issue, Dr. Hill thought. He saw nothing inconsistent with group practice in continuing a method of remuneration within the health center which bore a relationship to the amount of work done. On the whole, he said, there was much that was sound and attractive in the health center conception, but the attitude of the profession must be tinged with caution lest, without sufficient experiment, the project be pushed by those who sought not health centers but a particular form of salaried employment under local authorities.

Two things, he said, made Dr. Hill suspicious. The consent of the Central Medical Board was necessary before new practitioners could participate in the service or existing practitioners start in new areas. The argument was that practitioners must be prevented from going into areas already sufficiently staffed. There might be a case for that, Dr. Hill acknowledged, but the White Paper advocated that such approval must be given to every practitioner desiring to enter the public service. The board is to be a civil service structure under the general direction of the minister. Again, newly qualified doctors will be required to give full time in the public service in their early years if necessary. The association, Dr. Hill felt, was not prepared to accept this form of civil direction and conscription. He pointed to the danger that by administrative procedure, bit by bit, the one thing to which the profession was fundamentally opposed—a whole time salaried service—could be introduced.

The proposals of the White Paper will soon be discussed in Parliament. It is evident that any opposition from the medical profession will be in connection with such details as are mentioned here. Every proposal is open to debate before it becomes law.

BOLIVIA

(From Our Regular Correspondent)

La Paz, Feb. 21, 1944.

Typhoid Epidemic in La Paz

During the last two months there has been a severe epidemic of typhoid in Bolivia's largest city, La Paz. A minor epidemic developed in Cochabamba. Official estimates, based on doctors' reports, indicate that there have been about 200 cases and some 50 deaths, but private estimates place both figures about four times as high because of hidden cases. Lack of sanitary supervision over the open market sellers of vegetables, fruit and meat, the lack of good general hygienic conditions and the deficient sewage disposal systems in some suburbs are chiefly responsible for the fast spread of the epidemic, which apparently spreads from undetected sources every few years. Local health authorities have proceeded with immediate vaccination with Bolivian made vaccines, but out of a population of about 300,000 people only a few presented themselves. Also the Servicio Cooperativo Interamericano de Salud Pública, supported by the office of the coordinator of Inter-American affairs, vaccinated with American made vaccines, but it seems that a large number of people did not report for revaccination. The General Hospital isolation ward, with 51 beds available, soon became overcrowded. Fortunately, La Paz drinking water is acid, with an estimated p_H of from 5 to 6, so that no contamination occurred this way. The public was instructed by newspapers and radio about the safety measures to be adopted. Lack of available funds makes it hard to carry out any thorough measures against future epidemics of this kind.

A Branch of the International College of Surgeons in Bolivia

On January 12 the Bolivian branch of the International College of Surgeons was founded in La Paz in the presence of the former United States ambassador to Bolivia, Mr. Pierre de Boale, and the vice president of La Paz University, Dr. Ernesto Navarro. The chairman of this new institution, Dr. Enrique St. Loup, in his inauguration speech mentioned that the Bolivian branch of the institution was founded in response to an invitation received a year ago from the headquarters of the college in Washington, D. C. The program of this first meeting included the exhibition of a La Paz film showing the different phases of a subtotal thyroidectomy.

Deaths

John Henry Hale, Nashville, Tenn.; Meharry Medical College, Nashville, 1905; professor and chairman of the department of surgery at his alma mater, where he had been associate director of the tumor clinic; past president of the National Medical Association; served as medical director of the health department at the Tennessee State College; at one time surgeon in chief at the Millie E. Hale Hospital; was to have been awarded a Distinguished Service Medal this month at the John A. Andrew Clinic at Tuskegee Institute, Ala., for outstanding contributions to the Negro medical profession; chairman of the hospital committee and chief, surgical department, George W. Hubbard Hospital of Meharry Medical College, where he died March 27, aged 62, of myocardial insufficiency.

Arnold Schwyzer ✠ St. Paul; Universität Zürich Medizinische Fakultät, Switzerland, 1888; member of the founders group of the American Board of Surgery; professorial lecturer emeritus at the University of Minnesota Medical School, Minneapolis; formerly professor of clinical surgery at the Minneapolis College of Physicians and Surgeons, the Medical Department of Hamline University; member of the Minnesota Pathological Society, Minnesota Academy of Medicine, Swiss Surgical Society, American Surgical Association and the Western Surgical Association; fellow of the American College of Surgeons; for many years surgeon on the staff of St. Joseph's Hospital; died February 19, aged 79, of carcinoma of the pancreas.

Peter Lyons Harvie ✠ Troy, N. Y.; Harvard Medical School, Boston, 1911; a member of the founders group of the American Board of Surgery; formerly instructor in surgery at the Albany Medical College, Albany; fellow of the American College of Surgeons; served in the medical corps of the U. S. Army on the Mexican border and as a captain, commanding ambulance company number 5, third division, American Expeditionary Forces, in France during World War I; surgeon, Samaritan Hospital, Eddy Memorial Foundation and Day Home Clinic; thoracic surgeon, Pawling Sanatorium, Wynantskill; consulting surgeon, Henry W. Putnam Memorial Hospital, Bennington, Vt.; died February 4, aged 58, of heart disease.

Cyril Sumner ✠ Rochester, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1911; served as consultant in general surgery and instructor in surgery at the University of Rochester School of Medicine and Dentistry; past president of the Rochester Academy of Medicine; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons; served during World War I; director of the surgical department, Genesee Hospital; attending surgeon, Monroe County Hospital; for many years on the staff of the Strong Memorial Hospital; died February 7, aged 61, of diverticulitis.

Louis Provance McCormick ✠ Connellsville, Pa.; Jefferson Medical College of Philadelphia, 1891; retired from the Pennsylvania National Guard in 1915 with the rank of lieutenant colonel after twenty-one years of service; served during the Spanish-American War and the Philippine Insurrection; chairman of the Fayette County Draft Board number 2 during World War I and the Fayette County Selective Service Board number 1 during World War II; on the staff of the Connellsville State Hospital; treasurer, board of directors, Carnegie Free Library, and director of the Second National Bank; died February 6, aged 77, of angina pectoris.

Robert J. Walker ✠ Saugatuck, Mich.; Trinity Medical College, Toronto, Ont., Canada, 1895; past president of the Allegan County Medical Society and the Ottawa County Medical Society; first lieutenant in the medical corps of the U. S. Army during World War I, serving as commanding officer of a hospital train; at one time village health officer and member of the school board; on the staff of the Allegan Health Center, Allegan, and formerly on the staff of the Community Hospital, Douglas; for many years a director and president of the Fruit Growers State Bank; died February 1, aged 74, of lymphatic leukemia.

Raymond Welsh Holt ✠ Niagara Falls, N. Y.; University of Buffalo School of Medicine, 1928; specialist certified by the American Board of Pediatrics, Inc.; member of the American Academy of Pediatrics; served overseas with the American Expeditionary Forces during World War I; attending pediatrician, Mount St. Mary's and Niagara Falls Memorial hospitals; formerly on the staff of the Children's Hospital, Buffalo; director, board of Beeman Foundation Child Guidance Clinic; member of the Rotary Club; died in the Buffalo General Hospital, Buffalo, February 4, aged 50, following an operation.

Fred Meade Anderson, Nickerson, Kan.; St. Louis University School of Medicine, 1904; member of the Kansas Medical Society; died in St. Elizabeth Mercy Hospital, Hutchinson, January 17, aged 64, of cerebral hemorrhage.

John Ashburton Cutter, New York; Albany Medical College, New York, 1886; joint author of "Food: Its Relation to Health and Disease"; died in St. Vincent's Hospital February 13, aged 80, of arteriosclerotic heart disease, cerebral arteriosclerosis and bronchopneumonia.

George Bernard Grady, Watervliet, N. Y.; Albany Medical College, 1896; at one time a druggist; for many years medical supervisor of the schools and police surgeon; served as health officer; on the staff of the Troy Hospital, Troy; died February 15, aged 73, of heart disease.

Henry Hill Haskell, Carmel, Calif.; Harvard Medical School, Boston, 1893; served as assistant in ophthalmology at his alma mater; formerly a member of the American Ophthalmological Society and the New England Ophthalmological Society; for many years on the staff of the Massachusetts Charitable Eye and Ear Infirmary, Boston; died February 14, aged 75, of pulmonary edema and acute dilatation of the heart.

William Ellery Hughes ✠ Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1880; at one time professor of clinical medicine at the Medico-Chirurgical College of Philadelphia; consulting physician to the Philadelphia General, Misericordia and Presbyterian hospitals; accompanied Admiral Robert E. Peary on one of his early polar expeditions; died March 16, aged 87, of arteriosclerotic cardiopathy.

Sidney Hughes Jacobs, Atlanta, Ga.; Atlanta College of Physicians and Surgeons, 1910; formerly passed assistant surgeon in the U. S. Public Health Service reserve; served during World War I; died February 15, aged 60, of coronary thrombosis.

Sherman Williott Jenkins, Detroit; Meharry Medical College, Nashville, Tenn., 1926; on the staffs of the Wayne Diagnostic and Parkside hospitals; died in Jackson, Mich., February 20, aged 47, of coronary occlusion.

Christopher George Johnson ✠ Milwaukee; Trinity Medical College, Toronto, Ont., Canada, 1895; died February 18, aged 73, of myelogenous leukemia.

John Frank Johnson, Chicago; Jenner Medical College, Chicago, 1903; died February 19, aged 72, of chronic myocarditis.

Edward Charles Jones ✠ Montclair, N. J.; Tufts College Medical School, Boston, 1927; member of the American Society of Anesthetists, Inc.; on the staffs of the Mountainside, Community and St. Vincent's hospitals, Montclair, and the Essex County Hospital for Contagious Diseases, Belleville; died February 16, aged 52, of congestive heart disease.

Henry Turner Kendall, Columbia, S. C.; Hospital College of Medicine, Louisville, Ky., 1889; died in the Columbia Hospital February 21, aged 83, of pneumonia.

Herbert L. Lake, Lyons, N. Y.; Eclectic Medical Institute, Cincinnati, 1882; died January 30, aged 83, of chronic nephritis and arteriosclerotic heart disease.

Charles C. Landon, Battle Creek, Mich.; the Hahnemann Medical College and Hospital, Chicago, 1885; member of the Michigan State Medical Society; on the staffs of the Leila Y. Post Montgomery and the Community hospitals; formerly a member of the board of education and president of the Y. M. C. A.; died February 7, aged 84, of diabetes mellitus.

Charles Edwin Legg ✠ South Sioux City, Neb.; Kansas City (Mo.) Hahnemann Medical College, 1904; served in France during World War I; on the staff of the Methodist Hospital, Sioux City, Iowa; surgeon for the Burlington Railway; died February 15, aged 68, of coronary occlusion.

Theophilus H. Littell, Ville Platte, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1898; for many years coroner of Evangeline parish; died February 11, aged 69, of coronary thrombosis and cardiac insufficiency.

David Livingstone ✠ Centralia, Wash.; Trinity Medical College, Toronto, Ont., Canada, 1904; served during World War I; captain in the medical reserve corps of the U. S. Army, not on active duty; formerly medical superintendent of the Western State Hospital, Fort Steilacoom; died February 15, aged 65, of hypostatic pneumonia following influenza.

James C. MacGregor, Flint, Mich.; Detroit College of Medicine, 1898; also a pharmacist; member of the Michigan State Medical Society; past president of the Genesee County Medical Society; member of the board of managers of the Hurley Hospital for many years; served on the board of directors of the Industrial Savings Bank, the Union Industrial Trust and Savings Bank and the National Bank of Flint; died February 29, aged 72, of cardiac thrombosis.

Finley Joseph McRae ✠ Albion, Neb.; Western University Faculty of Medicine, London, Ont., Canada, 1902; secretary of the Boone County Medical Society; served as a captain in the medical corps of the U. S. Army during World War I; a director of the Nebraska Tuberculosis Association; past president of the Kiwanis Club; died in Our Lady of Lourdes Hospital, Norfolk, January 5, aged 67, of cerebral hemorrhage.

Hovsep Hagop Mahdesian, Fresno, Calif.; American University of Beirut School of Medicine, Syria, 1908; died in St. Agnes Hospital February 3, aged 60, of complications due to a duodenal ulcer.

Jacob Earl Meengs ✠ Grand Rapids, Mich.; Rush Medical College, Chicago, 1904; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; died February 2, aged 62, of valvular heart disease, arteriosclerosis and general edema with pleuritic effusion on the right side.

Charles A. Moore, Tampa, Fla.; Eclectic Medical Institute, Cincinnati, 1885; died in the Tampa Municipal Hospital February 6, aged 84, of cerebral hemorrhage.

Louis Grant Morrill, St. Clair, Mich.; Northwestern University Medical School, Chicago, 1913; member of the Michigan State Medical Society; formerly clinical assistant, instructor and associate in surgery at his alma mater; for many years on the staff of St. Luke's Hospital, Chicago, and had also been connected with the Commonwealth Edison Company in Chicago; died in the University Hospital, Ann Arbor, February 1, aged 65, of cerebral hemorrhage.

Solomon B. Myers, Mount Holly Springs, Pa.; Chicago Homeopathic Medical College, 1887; on the courtesy staff of the Carlisle Hospital, Carlisle, where he died February 1, aged 89, of myocardosis due to arteriosclerosis.

Henry Joseph Noerling ✠ Valatie, N. Y.; Albany Medical College, 1911; mayor of the village of Valatie; president of the Columbia County Board of Health and the Valatie Savings and Loan Association; member of the board of trustees of the National Union Bank of Kinderhook; on the staffs of the Hudson City Hospital, Hudson, and the Albany Hospital, Albany; died February 4, aged 55, of hypertension and myocardial degeneration.

George Henry Palmerlee, Detroit; Detroit College of Medicine, 1903; member of the Michigan State Medical Society; fellow of the American College of Surgeons; veteran of the Spanish-American War; served as a major in the National Guard; formerly medical inspector of the city board of health; on the staff of the Grace Hospital, where he died January 22, aged 71, of coronary thrombosis.

Don V. Poindexter, East St. Louis, Ill.; Marion-Sims College of Medicine, St. Louis, 1898; served one term as coroner of Bond County; died in St. Mary's Hospital, January 9, aged 69, of myocarditis and bronchiectasis.

Walter S. Quaintance, Slate Mills, Va.; University College of Medicine, Richmond, 1904; also a dentist; died in the University of Virginia Hospital, University, February 3, aged 62, of coronary thrombosis.

James Thomas Rainer ✠ Yazoo City, Miss.; Memphis (Tenn.) Hospital Medical College, 1912; member of the Mississippi State Medical Association; county physician; served overseas during World War I; on the staffs of King's Daughters Hospital and the Yazoo Clinic and Hospital; died February 3, aged 54, of cardiovascular renal disease.

Walter R. Schmidt, Glencoe, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1903; member of the Minnesota State Medical Association; served as coroner and health officer; clerk of school board at Chisholm; on the staff of Glencoe Municipal Hospital; died January 20, aged 65, of carcinoma with metastasis in the left axilla.

Samuel S. Shorer, Milwaukee; Bennett College of Eclectic Medicine and Surgery, Chicago, 1885; died January 5, aged 81, of influenza, acute bronchitis, arteriosclerosis and cardiorenal disease.

Edward Sylvester Smith, Bridgeport, Conn.; New York Homeopathic Medical College and Hospital, New York, 1888; served as president of the board of directors of the Y. M. C. A.; died in the Dr. J. H. Evans' Private Hospital, New Haven, February 4, aged 86, of arteriosclerotic heart disease and chronic arthritis.

William Thomas Stewart, Oxford, Ohio; Medical College of Ohio, Cincinnati, 1908; member of the Ohio State Medical Association; served in France as a captain in the medical corps of the U. S. Army during World War I; past president of the Butler County Board of Health; on the staffs of the Fort Hamilton Hospital and the Mercy Hospital, Hamilton, where he died January 23, aged 65, of Paget's disease and uremia.

Charles Midwood Stiles, Philadelphia; Medico-Chirurgical College of Philadelphia, 1898; member of the Medical Society of the State of Pennsylvania and the American Academy of Ophthalmology and Otolaryngology; served as a captain in the medical corps of the U. S. Army during World War I; for many years on the staff of the Frankford Hospital; died in the Veterans Administration Facility, Coatesville, January 27, aged 77, of bronchopneumonia.

James Milton Still, Dallas, Texas; Marion-Sims College of Medicine, St. Louis, 1892; past president of the Kaufman County Medical Society; at one time health officer of Kaufman County; died January 27, aged 74, of carcinoma of the buccal cavity.

Benjamin Early Stockwell ✠ St. Louis; Barnes Medical College, St. Louis, 1904; died February 2, aged 80, of heart disease.

William Veazey, Van Alstyne, Texas; University of Louisville (Ky.) Medical Department, 1898; for many years a member of the local school board; died in San Antonio January 27, aged 69, of cerebral arteriosclerosis.

Levin West ✠ Frederick, Md.; University of Maryland School of Medicine, Baltimore, 1886; served on the staffs of the Schnauffer Hospital, Brunswick, and the Frederick City Hospital; died January 30, aged 79, of cerebral embolism.

Clarence John Wichser, New Orleans; Tulane University of Louisiana School of Medicine, New Orleans, 1920; member of the Louisiana State Medical Society; physician in chief, city sewerage and water board; died in the Mercy Hospital January 25, aged 52, of cardiac infarct.

DIED WHILE IN MILITARY SERVICE

Frank Bolles Wakeman ✠ Colonel, M. C., U. S. Army, Washington, D. C.; Indiana University School of Medicine, Indianapolis, 1926; graduated in pharmacy, Valparaiso University in 1915, received degree in pharmaceutical chemistry, 1916, and the degree of bachelor of science, 1917; served in World War I from August 1917 to May 31, 1919, as a first lieutenant, infantry, Officers Reserve Corps; overseas with the 369th U. S. Infantry (old fifteenth New York Infantry); on active duty as a first lieutenant, medical reserve corps from Aug. 1, 1926 to Aug. 21, 1927, during which time he completed an internship at Walter Reed General Hospital; practiced medicine in Indiana from August 1927 to May 1928; appointed as a first lieutenant in the medical corps, regular army, on March 23, 1928; promoted to captain on June 3, 1928, major, June 4, 1937, temporary lieutenant colonel on Feb. 1, 1942 and temporary colonel on Sept. 8, 1942; graduate from basic course, Army Medical School, 1929, and advanced course, 1936; graduate from basic course, Medical Field Service School, Carlisle Barracks, 1929, and advanced course, 1938; served as an instructor in biochemistry at Army Medical School, 1932-1936, and instructor in sanitation at Medical Field Service School, 1937-1939; received the degree of master of arts in 1933 and the degree of doctor of philosophy in 1935 from Catholic University of America and the degree of doctor of public health in 1937 from Johns Hopkins University School of Public Health; graduated from the Command and General Staff School, Fort Leavenworth, Kan., in 1940; awarded the Henry Wellcome prize in 1938 by the Association of Military Surgeons of the United States for his essay on "A Specific Somatic Polysaccharide as the Essential Immunizing Antigen of the Typhoid Bacillus"; chief of the Training Division, Office of the Surgeon General, since February 1940; member of the Association of Military Surgeons of the United States and the Society of American Bacteriologists; fellow of the American College of Physicians; died in Fort Monmouth, N. J., March 17, aged 47, of coronary occlusion, while attending a conference of G-3 officers.

Correspondence

THE HISTORY OF PENICILLIN

To the Editor:—It is not too early to take considerable care in recounting the history of the development of penicillin. The remarkably rapid increase of professional as well as public interest in this potent but nontoxic bactericide dictates such caution. The full story of its rediscovery by Florey, Chain and their co-workers nine years after its original discovery by Fleming in 1929 has not yet been fully recorded. This is probably largely because Professor Florey has not wanted to detract from the honor due Prof. Alexander Fleming, its original discoverer, who is still living and still a brilliant observer. This is only just, but the lack of a full account of its rediscovery can lead to mistaken notions. Thus Herrell writes in THE JOURNAL, March 4, "Following the isolation of an antibacterial agent, gramicidin, from Bacillus brevis by Dubos in 1939, a reinvestigation of substances of biologic origin was naturally undertaken. Chain and other Oxford investigators in 1940 reported on penicillin and its possibilities as a chemotherapeutic agent." This statement appears to suggest that the rediscovery of penicillin at Oxford was stimulated by the development of gramicidin. This was not the case. Actually is was work on a less well known antibacterial agent, lysozyme, that had most to do with creating interest in penicillin at the Sir William Dunn Institute of Pathology.

Lysozyme, which also was discovered by Fleming, is a potent antibacterial enzyme found in most body tissues. It occurs in high concentration in human tears, in human saliva and particularly in egg-white. Egg-white lysozyme has been crystallized and found to be a carbohydrate-splitting enzyme. Before the development of gramicidin it was perhaps the best known of all the antibacterials of cellular origin. Florey had been interested in it for some time and had published on it as early as 1930.

In the fall of 1937 I came to Oxford as a Rhodes scholar to work in Florey's laboratory. He assigned me my doctorate thesis subject, "The Actions of Certain Bacteriolytic Principles," allowed me to choose Dr. Ernest Chain, a brilliant biochemist, as my supervisor, and bade me get to work to isolate the substrate of lysozyme. We did succeed in doing this, confirming and extending the findings of Karl Meyer and his co-workers. During the course of this work we began to share Florey's interest in other antibacterials of cellular origin, such as pyocyanin, actinomycin, streptothricin and bacteriophage. We read Fleming's original 1929 paper on penicillin, were most impressed with the possibilities of the subject and found it difficult to understand why the study of penicillin had practically lapsed for nine years. It appeared that this was probably due mainly to the difficulties in purification of the substance and not because the observations had not been confirmed.

We were very fortunate in being able to borrow a strain of the Fleming Penicillium notatum from another research investigator in the Sir William Dunn School of Pathology, Miss Campbell-Renton. She had kept the original Fleming strain going, hoping to work on penicillin sometime when her bacteriophage studies with Prof. A. D. Gardner did not claim all her time. With Florey's permission, Chain and I recultured this strain and tested the antibacterial properties of the medium on several cocci. The results were not impressive. Preliminary experiments rarely are. It was a particularly busy moment in the lysozyme research, so Professor Florey asked Dr. Norman Heatley to work with Chain on the further development of penicillin. This was in 1938, as I recall. Heatley and Chain, with the active advice of Professor Florey, succeeded in purifying and standardizing penicillin, and by the late spring of 1940 hard work had produced enough partially purified penicillin for use in animal experiments. These experiments were well planned and were immediately and brilliantly successful. Classically dramatic results were obtained. The importance of the findings was understood at once, and practically the whole Sir William Dunn Institute of Pathology was turned over to penicillin research, the work being financed mainly by the British Medical Research Council. It is a tribute to the wisdom of British science and to the British people as a whole that all this was accomplished at exactly the period of the greatest peril to their country—when France capitulated and when it appeared possible that the Nazis would invade England itself. The development of the clinical use of penicillin grew rapidly, and Professor Florey's visit to the United States in the summer of 1941 stimulated interest in it here. Commercial production was undertaken, with what results is now well known. It has been wisely shepherded by the National Research Council and given only to qualified investigators.

As will be obvious from the preceding account, my contact with the development of penicillin was largely tangential, although I did have the opportunity to work with it again under Prof. Warfield T. Longcope and Dr. Murray Fisher during my internship at the Johns Hopkins Hospital. It has been possible for me to observe, however, various steps in its development. That is why I am impelled to enumerate a few facts about its development at Oxford.

LESLIE A. FALK, 1st Lieutenant, M. C., A. U. S.

TOXICITY OF SODIUM BENZOATE

To the Editor:—With the increasing use of the synthesis of hippuric acid as a test of liver function, the toxicity of sodium benzoate requires careful revaluation. Recently Kinsey and Wright (*J. Lab. & Clin. Med.* **29**:188 [Feb.] 1944) reported that, after a patient recovering from a serious attack of hepatitis had taken the usual dose of 6 Gm. of sodium benzoate as used in the test, a strong reaction ensued: severe substernal pain, shock, increased icterus and later granulocytopenia and eosinophilia. To my knowledge this is the first severe reaction from sodium benzoate reported in the literature, although I have been informed of several cases in which untoward reactions to this drug were shown.

Sodium benzoate, generally speaking, is one of the most innocuous drugs known. Some of the older clinicians, Senator, for instance, gave doses of 12 Gm. daily to their rheumatic patients. Several investigators reported taking 40 Gm. or more of sodium benzoate in twenty-four hours with no pronounced toxic effect. I, as well as many others, have performed the hippuric acid test on patients with severe acute hepatitis without any demonstrable reaction.

In view of these observations, it seems clear that sodium benzoate has little or no direct toxic action other than occasionally causing nausea. When, therefore, a severe reaction occurs, a hypersensitivity has in all probability developed. Since benzoic acid lacks reactive groups in the ring, it is unlikely that it per se acts as a hapten. Since only about 80 per cent of the ingested benzoic acid is recovered as hippuric acid, it seems fairly certain that some of the compound is metabolized, and it is probable that a metabolic product, perhaps a hydroxybenzoic acid or a phenol, may be the factor to which the organism has become hypersensitive. This appears all the more likely in view of the fact that the patient of Kinsey and Wright had his toxic reaction not immediately but four hours after the sodium benzoate had been given. Since considerable benzoic acid is taken into the body almost daily in the food either as such or as quinic acid, which is converted to benzoic acid, sensitivity to benzoic acid must be exceedingly rare. It therefore seems justifiable to state that the danger of a serious reaction from sodium benzoate is so remote that one need not hesitate to do the oral hippuric

acid test whenever the information that this test supplies is deemed desirable.

The intravenous modification has been used extensively in various clinics and hospitals for the past few years. The incidence of untoward reactions is somewhat higher, but except for a few isolated instances the reactions have been transient. It is likely that many of these reactions are on a psychic basis brought on by the fact that the injection requires about five minutes, and that a cramplike pain may be produced if the solution is administered too fast. It should be emphasized that only a properly prepared solution of sodium benzoate be injected. Unless one has all the facilities to make solutions safe for intravenous administration, it is advisable to use commercial ampules prepared for the test.

While toxic reactions from sodium benzoate are rare, it is nevertheless important to know that they can occur, since forewarned is forearmed. The desirability of reporting toxic effects from sodium benzoate as well as from other drugs cannot be overstressed, since this is the only means whereby the relative safety of any drug can be accurately evaluated.

ARMAND J. QUICK, M.D., Milwaukee.

LATE MUSCLE ATROPHY IN POLIOMYELITIS

To the Editor:—In the issue of March 4, page 676, the answer to a query on the relationship of poliomyelitis to late muscle atrophy denies any possible correlation between the two conditions and states that the latter condition would be due "to some new injury to or disease of the muscle or its corresponding nerve." However, a number of cases of chronic anterior horn cell atrophy of a noninflammatory nature (progressive muscular atrophy, progressive nuclear atrophy) have been described, which have followed after a variable interval an attack of poliomyelitis. This degenerative condition has usually been reported in persons who have exercised their muscles strenuously; in a mountain climber, for example, and I saw it appear in a ditch digger two years after a typical attack of poliomyelitis. Thus it does seem that in some individuals the original inflammatory lesion of poliomyelitis leaves a locus of least resistance, which later succumbs to a degenerative process, of which the results seem identical with those ordinarily described in progressive muscular atrophy. Pronounced muscular activity seems to play some role in the initiation of this atrophy.

LEO A. SPIEGEL, M.D., New York.

"IMMEDIATE CARE OF THE NEWBORN"

To the Editor:—This communication is in reference to the article on "Immediate Care of the Newborn in Relation to Neonatal Mortality," by Ralph M. Tyson, M.D., which appeared in THE JOURNAL, February 5.

In the section on skin infections he recommends that a 5 per cent lotion of sulfathiazole be applied freely. "Exposure to ultraviolet radiation at a close distance is helpful." Many dermatologists are seeing eruptions following the external use of sulfonamides in various vehicles. Many of us believe that their use is being overdone. This applies particularly to impetigo, in which ammoniated mercury is still preferred.

The sulfonamides are apt to produce sensitization just as much as and more so than ammoniated mercury. The sulfonamide compounds also sensitize the skin to the sun and I strongly advise against the concurrent use of ultraviolet rays that the author suggests—not only in impetigo but also in the treatment of any other disease. An article of mine in preparation cites the deleterious effects of ultraviolet rays applied to the skin after the topical application of sulfonamide ointment.

E. WILLIAM ABRAMOWITZ, M.D., New York.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, April 15, page 1153.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part I-II.* Various centers, May 1-3. Exec. Sec., Mr. E. S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGOLY: *Written.* Various large cities, May 8. *Oral.* Chicago, June 17. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* Chicago, June 8-10. Final date for filing application is May 20. *Written.* Various centers Oct. 16. Candidates in military service may take examination at their place of duty. Final date for filing application is August 15. Asst. Sec., Dr. W. A. Werrell, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY. Chicago, June 5. Sec., Dr. Paul C. Bucy, 912 S. Wood St., Chicago.

AMERICAN BOARD OF OBSTETRICS & GYNECOLOGY. *Oral. Part II.* Pittsburgh, June 7-13. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: New York, June 2-5. Chicago, Oct. 5-7. Sec., Dr. S. Judd Beach, 704 Congress St., Portland, Me.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral and Written. Part I.* Chicago, New Orleans, New York and San Francisco, October. Final date for filing application is August 1. Sec., Dr. G. A. Caldwell, 3503 Prytania St., New Orleans.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* New York City, June 1-4. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City, Ia.

AMERICAN BOARD OF PATHOLOGY: *Oral and Written.* Chicago, June 7-8. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: *Written.* Locally, Sept. 22. *Oral.* St. Louis, Nov. 8-9. Final date for filing application is Aug. 15. Sec., Dr. C. A. Aldrich, 115½ First Ave. S.W., Rochester, Minn.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Compensation of Physicians: Reasonableness of Fee for Mastoidectomy.—The physician plaintiff, an otologist, on June 19, 1937 performed a mastoidectomy on the patient for an infection involving the petrous portion. Beginning about six months later the physician made more than sixty visits to the patient, for what purpose the reported case is not clear but "not in connection with postoperative treatment." When the operation was performed the patient was a minor and arrangements for it were made by his uncle, who was told by the physician that the charge for the operation would be very moderate. In March 1938 the patient was emancipated by court judgment and subsequently inherited approximately $40,000 from the estate of his father. Apparently unaware of the inheritance, the physician billed the patient for $400 for the operation and $115 for subsequent visits. Between April 1939 and January 1940 the patient paid the physician a total of $80 on account and sent him letters in which he expressed appreciation for the consideration shown him, admitted the bill was fair, and stated his intention to pay as soon as he could. Subsequently the physician sued the patient for the unpaid balance. The patient defended by claiming that the amount charged for the operation was excessive and that the sixty or more professional visits for which charges had been made "were made necessary because of postoperative treatment" for which no additional charges should have been made. From a judgment, in the main, for the physician the patient appealed to the court of appeal of Louisiana, Orleans Parish.

The appellate court held that the amount charged for the operation was not excessive in view of the testimony of two "recognized otologists," called as witnesses by the physician at the trial, to the effect that the performance of a mastoidectomy "for a petrous infection" was most serious and that a charge of $400 for such an operation would be the minimum which should be charged. Even though the physician, said the court, may have told the patient's uncle that the charge would be very moderate, surely the physician did not intend to give the impression that he would make no charge at all but merely that he would make the minimum charge usual for such an operation. In determining what is a correct charge for professional services, there should be considered two things: first, the training and experience necessary and the seriousness of the treatment or operation; and, second, the ability of the defendant to pay. We do not mean that because a defendant may be a very rich man he may be required to pay an exorbitant charge, but we do mean that, where a defendant is shown to be well able to pay, the physician should not be required to reduce his charge and in fixing it may take into consideration the fact that the patient has ample funds out of which to make the payment.

At the trial, to prove the reasonableness of the charge made for the operation, the physician called the two otologists referred to, who heard all of the evidence at the trial. At the close of the evidence, counsel for the plaintiff asked for a rule on the defendant to tax the witness fees of these two otologists as costs of court and asked that those fees be fixed at $50 each. Counsel for the defendant contended that these charges should not be taxed as costs of court first, because the testimony was not expert evidence and, secondly, because in support of the rule to tax their fees the two experts themselves did not take the witness stand but merely submitted bills to the court. The patient contended that the testimony of the otologists was not expert testimony because no special study or experience in any branch of science was necessary to give the testimony they gave. The patient called attention to a Louisiana statute which provides that witness fees, in addition to the fees allowable to an ordinary witness, may be allowed by the court with respect to a witness called to testify only to an opinion founded on special study or experience in any branch of science. (Dart's Revised Statutes, vol. 1, sec. 1990). The patient argued that any layman who had employed a physician may testify as to what the charge made against him was and from such experience might testify as to what such charges should be. We cannot agree with this contention, said the appellate court. It is true that any layman who has required the services of a physician may know what charge was made against him and it is true that any layman who has required such services often may have acquired experience which will enable him to judge, with fair accuracy, just what charge will be made for any given services. However, only one who has himself had experience in rendering the same kind of service or in performing the same kind of operation or who has had experience in making charges therefor may be said to be capable of giving expert testimony on the subject. Where the bill of a physician is questioned, the best evidence as to its correctness must be given by another physician who has himself studied the same branch of science and knows how serious may have been the condition of the patient, or how dangerous may have been the operation. The court accordingly concluded that the two otologists gave expert testimony and that therefor their fees as experts should be taxed as costs of court if properly proved. The court, however, held that their fees were not properly proved since they did not take the witness stand and thus submit themselves to cross examination but only submitted bills to the court. The court held that the witness fees of the otologists could not be allowed at this time.

The judgment in favor of the physician for the unpaid balance of his charges for the operation and the subsequent visits was affirmed.—*Womack v. Burka, 14 So. (2d) 302 (La., 1943).*

Society Proceedings

COMING MEETINGS

American Medical Association, Chicago, June 12-16. Dr. Olin West, 535 N. Dearborn St., Chicago 10, Secretary.

American Association for the Surgery of Trauma, Chicago, June 9-10. Dr. Gordon M. Morrison, 520 Commonwealth Ave., Boston, Secretary.

American Association for Thoracic Surgery, Chicago, May 5-6. Dr. Richard H. Meade Jr., Kennedy General Hospital, Memphis, 15, Tenn., Secretary.

American Association of Genito-Urinary Surgeons, Stockbridge, Mass., June 8-10. Dr. Charles C. Higgins, 2020 E. 93d St., Cleveland, Secretary.

American Association of Industrial Physicians and Surgeons, St. Louis, May 8-11. Dr. Edward C. Holmblad, 28 East Jackson Blvd., Chicago, Managing Director.

American Association of Plastic Surgeons, Philadelphia, May 25-27. Dr. Frederick A. Figi, 102 Second Ave., S.W., Rochester, Minn., Secretary.

American Association on Mental Deficiency, Philadelphia, May 11-15. Dr. Neil A. Dayton, Mansfield Training School, Mansfield Depot, Connecticut, Secretary.

American Broncho-Esophagological Association, New York, June 6. Dr. Paul H. Holinger, 700 N. Michigan Ave., Chicago, Secretary.

American College of Radiology, Chicago, June 14. Mr. Mac F. Cahal, 540 N. Michigan Ave., Chicago, Secretary.

American Diabetes Association, Chicago, June 11. Dr. Cecil Striker, 630 Vine St., Cincinnati 2, Secretary.

American Gastro-Enterological Association, Chicago, June 12-13. Dr. J. Arnold Bargen, 102 Second Ave. S.W., Rochester, Minn., Secretary.

American Laryngological Association, New York, June 7-8. Dr. Arthur W. Proetz, 3720 Washington Blvd., St. Louis, 8, Secretary.

American Laryngological, Rhinological and Otological Society, New York, June 9-10. Dr. C. Stewart Nash, 277 Alexander St., Rochester, N. Y., Secretary.

American Medical Women's Association, Chicago, June 10-11. Dr. Carroll L. Birch, 2045 Sedgwick St., Chicago, Secretary.

American Neurological Association, New York, May 19-20. Dr. Henry Alsop Riley, 157 E. 72d St., New York 21, Secretary.

American Ophthalmological Society, Hot Springs, Va., May 29-31. Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y., Secretary.

American Proctologic Society, Chicago, June 11-15. Dr. W. H. Daniel, 1930 Wilshire Blvd., Los Angeles 5, Secretary.

American Psychiatric Association, Philadelphia, May 15-18. Dr. Winfred Overholser, St. Elizabeth's Hospital, Washington, D. C., Secretary.

American Psychoanalytic Association, Philadelphia, May 13-15. Dr. Robert P. Knight, 3617 W. Sixth Ave., Topeka, Kansas, Secretary.

American Society for Clinical Investigation, Atlantic City, May 8. Dr. Wesley W. Spink, University Hospitals, Minneapolis, Secretary.

American Therapeutic Society, Chicago, June 10. Dr. Oscar B. Hunter, 1835 I St. N.W., Washington 6, D. C., Secretary.

Association for Research in Ophthalmology, Chicago, June 13. Dr. B. F. Payne, School of Aviation Medicine, Randolph Field, Texas, Secretary.

Association for the Study of Internal Secretions, Chicago, June 12-13. Dr. Henry H. Turner, 1200 N. Walker St., Oklahoma City, Secretary.

Association of American Physicians, Atlantic City, May 9. Dr. Joseph T. Wearn, Lakeside Hospital, Cleveland, Secretary.

California Medical Association, Los Angeles, May 7-8. Dr. George H. Kress, 450 Sutter Street, San Francisco 8, Secretary.

Connecticut State Medical Society, Bridgeport, May 2-4. Dr. Creighton Barker, 258 Church St., New Haven, Secretary.

Georgia, Medical Association of, Savannah, May 9-12. Dr. Edgar D. Shanks, 478 Peachtree St. N.E., Atlanta, Secretary.

Hawaii Territorial Medical Association, Honolulu, May 5-6. Dr. A. V. Molyneux, 1164 Punchbowl St., Honolulu, Secretary.

Illinois State Medical Society, Chicago, May 16-18. Dr. Harold M. Camp, 224 S. Main St., Monmouth, Secretary.

Kansas Medical Society, Topeka, May 10-11. Dr. F. R. Croson, 112 West Sixth Street, Topeka, Secretary.

Louisiana State Medical Society, New Orleans, April 24-26. Dr. P. T. Talbot, 1430 Tulane Ave., New Orleans, 13, Secretary.

Maryland, Medical and Chirurgical Faculty of, Baltimore, April 25-26. Dr. W. Houston Toulson, 1211 Cathedral St., Baltimore, Secretary.

Massachusetts Medical Society, Boston, May 23-24. Dr. Michael A. Tighe, 8 Fenway, Boston 15, Secretary.

Mississippi State Medical Association, Jackson, May 9-10. Dr. T. M. Dye, Box 995, Clarksdale, Secretary.

Missouri State Medical Association, Kansas City, April 23-25. Dr. Ralph L. Thompson, 634 N. Grand Blvd., St. Louis, Secretary.

National Tuberculosis Association, Chicago, May 10-12. Dr. Charles J. Hatfield 1790 Broadway, New York, Secretary.

Nebraska State Medical Association, Omaha, May 1-4. Dr. R. B. Adams, 416 Federal Securities Bldg., Lincoln, Secretary.

New Hampshire Medical Society, Manchester, May 16. Dr. C. R. Metcalf, 5 S. State St., Concord, Secretary.

New Jersey, Medical Society of, Atlantic City, April 25-27. Dr. Alfred Stahl, 58 Lincoln Park, Newark, Secretary.

New York, Medical Society of the State of, New York, May 8-11. Dr. Peter Irving, 292 Madison Ave., New York 17, Secretary.

North Carolina, Medical Society of the State of, Pinehurst, May 1-3. Dr. R. D. McMillan, P. O. Box 232, Red Springs, Secretary.

North Dakota State Medical Association, Fargo, May 7-9. Dr. L. W. Larson, 221 5th Street, Bismarck, Secretary.

Ohio State Medical Association, Columbus, May 2-4. Mr. Charles S. Nelson, 79 E. State St., Columbus, Executive Secretary.

Oklahoma State Medical Association, Tulsa, April 24-26. Dr. L. J. Moorman 1260 N. Walker St., Oklahoma City, Secretary.

Rhode Island Medical Society, Providence, May 24-25. Dr. William P. Buffum, 122 Waterman St., Providence 3, Secretary.

Society for Investigative Dermatology, Chicago, June 13. Dr. S. W. Becker, 55 E. Washington St., Chicago, Secretary.

Society of American Bacteriologists, New York, May 3-5. Dr. W. C. Frazier, 310 Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.

South Dakota State Medical Association, Huron, May 21-23. Dr. Roland G. Mayer, 22½ S. Main St., Aberdeen, Secretary.

Texas, State Medical Association of, Dallas, May 10-11. Dr. Holman Taylor, 1404 W. El Paso Street, Fort Worth, Secretary.

West Virginia Medical Association, Wheeling, May 15-16. Mr. Charles Lively, P. O. Box 1031, Charleston, Executive Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1934 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Orthopsychiatry, New York

14:1-190 (Jan.) 1944. **Partial Index**

Rorschach Test with Young Children. Anna Hartoch Schachtel.—p. 1.
Personality Development of Boy From Age 2 to 7. Lois Barclay Murphy.—p. 10.
Rorschach Method as Therapeutic Agent. G. R. Kamman.—p. 21.
Reactions of Children with Fathers and Brothers in Armed Forces. G. E. Gardner and H. Spencer.—p. 36.
Collective Psychotherapy of Mothers of Emotionally Disturbed Children. Fanny Amster.—p. 44.
Types of Personality Structure Encountered in Child Guidance Clinics. R. L. Jenkins and L. Hewitt.—p. 84.
Defective Delinquent: Definition and Prognosis. L. A. Lurie, S. Levy and Florence M. Rosenthal.—p. 95.
Mongolism Among School Children. J. E. W. Wallin.—p. 104.
"Opportunity" Class: Study of Children with Problems. J. W. Beckmann.—p. 113.
Psychiatric Problems in Training School for Delinquent Girls. Margaret C. L. Gildea.—p. 128.
Mental Hygiene Value of Children's Art Work. Maria Brick.—p. 136.
Danger and Morale. E. Kris.—p. 147.
Correlation Between Wechsler Mental Ability Scale, Form B, and Kent Emergency Test (E-G-Y) Administered to Army Personnel. E. D. Greenwood, H. L. Snider and M. M. Senti.—p. 171.

American Journal of Public Health, New York

34:1-100 (Jan.) 1944

Public Health Implications of Tropical and Imported Diseases: Strategy Against the Global Spread of Disease. T. Parran.—p. 1.
*Id.: Yellow Fever and Typhus and Possibility of Their Introduction into United States. W. A. Sawyer.—p. 7.
*Id.: Imported Malaria. O. R. McCoy.—p. 15.
Id.: Public Health Aspects of Certain Other Diseases to Which Our Military Forces May Be Exposed. H. E. Meleney.—p. 20.
*Immunizations in United States Army. A. P. Long.—p. 27.
Experience with Administrations of Medical Care Program for Wives and Infants of Enlisted Men. Martha M. Eliot.—p. 34.
Epidemiologic Notes on Meningococcal Meningitis in Army. P. E. Sartwell and W. M. Smith.—p. 40.
Objectives in Programming of Postwar Sanitation Works. E. Boyce.—p. 50.
The Battle for Health: Radio Script. I. Tunick.—p. 54.

Yellow Fever and Typhus: Possibility of Their Introduction into the United States.—Sawyer shows that the most serious risk of introducing yellow fever is through air travel. Travelers visiting infected regions have been encouraged to get themselves vaccinated. Passengers arriving from endemic areas are inspected by quarantine officers. Persons showing elevation of temperature or other evidence of illness are detained until a diagnosis is made. Those who are well and are nonimmune but who have possibly been exposed within a few days are kept under surveillance for the remainder of the incubation period of six days unless the destination is north of any region in which Aedes aegypti might breed. The control of Aedes aegypti remains the method of choice for cities and other places in the tropics and subtropics where this mosquito has become established. Aedes aegypti is especially vulnerable, as it is highly domestic and accessible and not so widely distributed as is commonly supposed. This makes it possible for health departments to organize a systematic attack on the mosquito in its larval stages and so hasten this dangerous insect on the way to local extermination. Most effective methods have been worked out in Brazil and applied with such success that in most cities and in many large areas Aedes aegypti can no longer be found. Introduction of louse borne typhus by returning troops would seem improbable. There are, however, other ways in which louse borne typhus can enter this country in time of war and spread as far as the local louse infestation will permit. The point is illustrated by the occurrence observed in the Southwest in 1916. The present situation in the United States with respect to the risks of typhus introduction is quite different from the one in 1916. All that protected us from a widespread epidemic of typhus during the last war was the general freedom of the public from body lice. As a rule the disease showed no tendency to spread beyond the immediate contacts of the persons introducing it into the communities. There is no reason to believe that lousiness is any more prevalent now than then or that war conditions will bring about a great increase in these insects.

Tropical and Imported Malaria.—McCoy emphasizes that large numbers of troops returned from overseas are infected with malaria. Although there is a hazard of the establishment of new foci of malaria infections of the country now free of the disease, the chances of serious consequences from such introduction are not considered very great. Prompt antimosquito measures should bring about rapid control of possible outbreaks. Intensification of anopheline mosquito control is indicated in the present endemic areas in this country to lessen the hazard from the introduction of new strains of malarial parasites. The most important problem connected with the return of military personnel infected with malaria is to insure proper diagnosis and treatment of the relapses which may occur after the service men have returned to their home communities.

Immunizations in the United States Army.—Long discusses the prevention of disease by immunization procedures. These immunizations have been divided into two classifications: the so-called routine immunizations and the special immunizations. The routine immunizations are those administered to all military personnel as soon as possible after entrance into the federal service. These are vaccinations against smallpox, typhoid and the paratyphoid fevers and active immunization against tetanus. Procedures referred to as special immunizations include vaccination against yellow fever, typhus and cholera. Vaccination against plague is another procedure for which provisions have been made. As in typhus and cholera, sanitary measures are stressed for the prevention of plague, and it is believed that in the majority of instances these measures will prove to be adequate protection. Plague vaccine is not now routinely administered to troops but is supplied to forces in areas where danger from the disease may be confronted. Immunization against such diseases as diphtheria and scarlet fever is not routinely practiced, but materials are made available for use if the situation should require artificial protection against these diseases.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

51:1-124 (Jan.) 1944

Roentgenologic Types of Pulmonary Lesions in Primary Coccidioidomycosis. J. R. Colburn.—p. 1.
Acute Phosgene Poisoning: Roentgen Findings in Lungs: Case Report. H. H. Sage.—p. 9.
Cholecystography and Jaundice. F. Huber.—p. 12.
Laminographic Studies of Aorta: Their Advantages and Limitations. W. G. Scott and D. S. Bottom.—p. 18.
Practical Cardiokymography: Its Significance in Evaluating Cardiac Function. L. J. Friedman and P. S. Friedman.—p. 29.
Angiocardiographic Analysis of Cardiac Configuration in Rheumatic Mitral Disease. A. Grishman, M. L. Sussman and M. F. Steinberg.—p. 33.
*Nontuberculous Pulmonary Cavitation. L. Nathanson and P. Morgenstern.—p. 44.
*Emphysematous Cholecystitis. C. A. Stevenson.—p. 53.
Roentgen Therapy for Bronchiogenic Cancer. B. P. Widmann.—p. 61.
Roentgen Study of Lymphogranuloma Venereum: Report of 24 Cases. I. Klein.—p. 70.
Data on Attentuation of Narrow and Broad Beams of 1,000 Kilovolt (Peak) Roentgen Rays by Lead, Concrete and Water. T. R. Folsom and Elizabeth F. Focht.—p. 76.
Three and One-Half Years' Experience with the 1,000 Kilovolt Roentgen Therapy Unit at Memorial Hospital. A. F. Hocker and Ruth J. Guttman.—p. 83.

Nontuberculous Pulmonary Cavitation.—Nathanson and Morgenstern illustrate roentgenographically lesions of the lung which presented cavitation or what simulated cavitation, particularly of the upper lobes, and which on biopsy or necropsy proved to be nontuberculous. The majority of these patients were referred to Sea View Hospital from other metropolitan hospitals with the diagnosis of tuberculosis made clinically, roentgenographically and in 1 instance apparently by a positive sputum examination. The authors present 8 cases with anthracosilicosis, cystic disease of the lung, actinomycosis, aortic aneurysm producing pulmonary necrosis, bronchogenic neoplasm with parenchymal necrosis, a lung abscess of the upper lobe, cavitation probably as a result of Friedländer's bacillus infection

of the lung, and a case of bronchiectatic cavitation of the upper lobe. Other lesions will produce cavitation in the lung, and Winn has recently reported 12 cases of pulmonary cavitation associated with coccidioidal infection. Slowly resolving nonspecific pneumonias may present areas of clearing that simulate cavitation, and one may find cysts or bleb formation in association with pneumonias in children which will suggest a tuberculous lesion. Occasionally a gumma may cavitate centrally and simulate tuberculosis. The authors stress that roentgenographic demonstration of cavitation is not conclusive for the diagnosis of pulmonary lesions and that the possibility of other pulmonary lesions must be kept in mind.

Emphysematous Cholecystitis.—Stevenson defines emphysematous cholecystitis as an acute infection of the gallbladder characterized by gas production in the gallbladder lumen, walls and pericholecystic tissues. Any virulent gas-producing organism may be responsible. Hegner in 1931 reported what apparently was the first case in which it was possible to make a preoperative diagnosis of this condition by means of roentgenography. Stevenson's 3 patients had roentgenologic aspects similar to Hegner's patient. All 3 were men, aged 64, 63 and 52 respectively. All 3 patients showed gas in the gallbladder, blebs in the wall and collections of gas in the pericholecystic tissues. No gas was noted within the biliary duct system. In 2 of the patients the condition was correctly diagnosed preoperatively. Medical treatment consisting of sulfathiazole, Clostridium welchi antiserum and roentgen radiation was successful in the treatment of 1 case. The author concludes that roentgenograms of the gallbladder region are of distinct value in cases of acute cholecystitis. The roentgenographic demonstration of gas in the gallbladder lumen, emphysematous blebs in the gallbladder wall and collections of gas in the pericholecystic tissues is indicative of acute gangrenous cholecystitis, most likely caused by Cl. welchi.

American Review of Tuberculosis, New York

49:115-202 (Feb.) 1944

*Silicotuberculosis. O. Auerbach and Marguerite G. Stemmerman.—p. 115.
Quantity of Focal (Tubercle) Calcium in Human Lungs. P. E. Steiner, D. W. Stanger, Miriam Bolyard and A. W. Marcovitch.—p. 129.
Tuberculous Stenosis of Major Bronchi: Its Diagnosis by Rhonchi, Verified by Bronchoscopy. M. McConkey and J. Gordon.—p. 140.
Sarcoidosis: One Case Report and Literature Review of Autopsied Cases. E. H. Rubin and M. Pinner.—p. 146.
Tuberculosis in Employed Women: Morbidity and Mortality Trends in Relation to Age. Martha V. Doran.—p. 170.
Effect of Yeast on Toxic Reactions of Promin on Tuberculous Guinea Pigs. G. M. Higgins and W. H. Feldman.—p. 179.

Silicotuberculosis.—To determine whether pneumonoconiosis alters or is itself altered by pulmonary tuberculosis, Auerbach and Stemmerman reviewed 54 cases of silicotuberculosis and compared them with 9 cases of pneumonoconiosis without tuberculosis and 200 cases of tuberculosis without pneumonoconiosis. They found that, although silicosis and tuberculosis exist concomitantly in the same lung, each maintains its individual integrity. Tuberculosis apparently does not alter the silicosis present. Pneumonoconiosis alters tuberculosis only to the extent that the silicotic nodules prevent the full development of tuberculous granulation tissue and, in the walls of cavities, the pyogenic membrane. Both granulation tissue and pyogenic membrane, however, are present in those portions of the lung where the silicotic foci are small or absent. Except for this quantitative difference they found little variation in the tuberculous process, whether or not pneumonoconiosis is present. The size, situation and number of cavities are approximately the same. There is a slightly greater incidence of perforation of cavities through the interlobar fissures in the silicotic and a greater incidence of death from fatal pulmonary hemorrhage. The latter factor is due to the greater productive reaction in the silicotic lung with greater opportunity to develop an aneurysm of a branch of the pulmonary artery. The authors found it difficult to determine the exact time at which pulmonary tuberculosis was superimposed on pneumonoconiosis unless the patient was under observation during the transition period, since the symptoms of the two diseases are similar. While fever and definite evidence of cavitation on roentgenography are useful diagnostic aids, the final conclusion must be based on the demonstration of the tubercle bacillus. Collapse therapy was of little value in cases of silicotuberculosis. This is apparently due to the fact that the silicotic lung remains voluminous and shows no tendency to collapse. Most patients succumbed to progressive pulmonary insufficiency. When the tuberculous process invaded the remaining portions of resilient lung tissue sufficiently, death was inevitable.

Archives of Internal Medicine, Chicago

73:1-112 (Jan.) 1944

Effect of Cinchophen on Secretion of Cholic Acid. J. H. Annegers, F. E. Snapp, A. C. Ivy and A. J. Atkinson.—p. 1.
Morgagni-Stewart-Morel Syndrome: Report of Case with Pneumoencephalographic Findings. M. T. Moore.—p. 7.
Effectiveness of Various Sulfonamide Drugs and Neoarsphenamine Against Pneumococci in Bone Marrow Cultures: Comparative Study. E. E. Osgood and J. G. M. Bullowa, with the technical assistance of I. E. Brownlees.—p. 13.
Capillary Fragility in Relation to Diabetes Mellitus, Hypertension and Age. S. B. Beaser, A. Rudy and A. M. Seligman.—p. 18.
Vitamin Therapy in Increased Capillary Fragility of Diabetes Mellitus. A. Rudy, S. B. Beaser and A. M. Seligman.—p. 23.
*Influence of Respiration on Blood Pressure in Man: with Note on Vasomotor Waves. A. Battro, R. González Segura, C. A. Eliçabe and E. Araya.—p. 29.
Rate of Sedimentation of Erythrocytes in Sickle Cell Anemia. T. Winsor and G. E. Burch.—p. 41.
Gastroenterology: Review of Literature from July 1942 to July 1943. C. M. Jones.—p. 53.

Influence of Respiration on Blood Pressure.—Battro and his associates studied the registration of the intra-arterial pressure of human subjects. They ascertained that under normal conditions two principal types of waves exist: (1) vasomotor waves, which are independent of the respiratory movements and should be called by the names of their discoverers, Traube and Hering, and (2) blood pressure waves depending on the respiratory movements (respiratory waves). The authors discuss the different factors which influence the production of these waves. The intra-arterial pressure has no uniform or fixed behavior during the respiratory movements but may rise or fall in accordance with the type of breathing—thoracic or abdominal—or with the frequency or depth of respiration. Even during ordinary breathing, slight changes are noticeable, the most constant being a fall of blood pressure during inspiration and an elevation during expiration. With deep, slow thoracic breathing there usually occur an inspiratory fall and an expiratory rise of the blood pressure. The opposite, as a rule, is true of abdominal breathing of the same type. Curves of intra-arterial pressure registered during inspiratory apnea and the Valsalva test show a definite fall of blood pressure at the beginning, while those taken during expiratory apnea are characterized by a slight initial fall and a terminal rise. Coughing causes great increase in the blood pressure.

Archives of Neurology and Psychiatry, Chicago

51: 113-212 (Feb.) 1944

Studies in Reflexes: History, Physiology, Synthesis and Nomenclature: Study I. R. Wartenberg.—p. 113.
Simple Method of Determining Frequency Spectrums in Electroencephalogram: Observations on Effects of Physiologic Variations in Dextrose, Oxygen, Posture and Acid-Base Balance on Normal Electroencephalogram. G. L. Engel, J. Romano, E. B. Ferris Jr., J. P. Webb and C. D. Stevens.—p. 134.
Electrodiagnosis by Means of Progressive Currents of Long Duration: Studies on Cats with Experimentally Produced Section of Sciatic Nerves. L. J. Pollock, J. G. Golseth, A. J. Arieff, I. C. Sherman, M. A. Schiller and E. L. Tigay.—p. 147.
Biopsies of Brain of Schizophrenic Patients and Experimental Animals. W. R. Kirschbaum and G. Heilbrunn.—p. 155.
Relation of Narcolepsy to Epilepsies: Clinical-Electroencephalographic Study. R. Cohn and B. A. Cruvant.—p. 163.
*Acetylcholine Treatment of Schizophrenia. L. H. Cohen, T. Thale and M. J. Tissenbaum.—p. 171.
Effect of Serum on Survival Time of Brain Tissue and Revival of Cerebral Oxidation. J. Wortis.—p. 176.
Injury to Peroneal Nerve Due to Crossing the Legs. H. S. Dunning.—p. 179.
Progressive Multiform Angiosis: Association of Cerebral Angioma, Aneurysms and Other Vascular Changes in Brain. S. Arieti and E. W. Gray.—p. 182.

Acetylcholine in Schizophrenia.—Cohen and his collaborators review the use of acetylcholine in the treatment of mental disease. Their studies were carried out on 11 patients. They describe a typical seizure that developed in 27 instances following the intravenous injection of 400 mg. of acetylcholine. A table lists age, duration of illness, number of treatments and

outcome in the 11 patients. The number of treatments varied between three and twenty-four. There was slight improvement in 1 woman, moderate improvement in another woman and remission in 1 man aged 36. The history of this last patient is described in detail. A total of twenty-four electric shock treatments had been ineffective. About five weeks after cessation of the electric treatments acetylcholine therapy was begun. Four treatments were given in all. The successive doses were 150, 300, 450 and 600 mg. The usual minor responses were noted during the first two treatments. He was pulseless for twenty seconds during the third treatment, with some twitching. During the fourth treatment he was several times pulseless for periods of from twenty to fifty seconds. After this therapeutic episode the dramatic remission took place. In 8 of 11 schizophrenic patients treated with convulsant doses of acetylcholine no general therapeutic benefit was obtained. The authors conclude that the therapeutic results do not justify the continued use of acetylcholine in this manner, particularly since the margin of safety of the drug appears to be extremely slight.

Archives of Surgery, Chicago

48:1-104 (Jan.) 1944

*Application of Dicoumarin (3,3'-Methylene-Bis-[4-Hydroxycoumarin]) in Trauma and Gangrene. C. E. Brambel and F. F. Loker.—p. 1.
Toxicopathologic Studies on Dye T-1824. W. C. Hueper and C. T. Ichniowski.—p. 17.
Goiter Heart: Experimental Study. C. A. Hellwig.—p. 27.
Hypoproteinemia: Clinical Relationship of Proteins and Protein Metabolism to Therapy with Special Reference to Surgery. A. O. Wilensky.—p. 36.
Reconstructive Plastic Surgery of Absent Ear with Necrocartilage: Autogenous Method. E. S. Lamont.—p. 52.
Review of Urologic Surgery. A. J. Scholl and others.—p. 73.
Progress in Orthopedic Surgery for 1942: Review Prepared by Editorial Board of American Academy of Othopedic Surgeons: XIV. Conditions of Foot and Ankle.—p. 89.

Dicumarol in Trauma and Gangrene.—Brambel and Loker used dicumarol and heparin in several cases. They treated (1) post-traumatic conditions with associated gangrene following crush injury, (2) diabetic and arteriosclerotic gangrene and (3) frostbite. Eleven cases are presented and analyzed. Without exception, all cases exhibited increased prothrombin activity, detectable in dilute plasma. This suggests an indication for the administration of hemorrhagic compounds to alter biochemical conditions favoring thrombus formation. The use of dicumarol in the treatment of granulating and ulcerative lesions is not contraindicated if caution and adequate control are exercised. Emphasis is placed on the value of frequent determinations of the prothrombin clotting time as an index to dosage. No set dosage for dicumarol was found in the cases presented. Some required much larger doses than others. No contraindications were found when sulfonamide compounds and the hemorrhagic agent (dicumarol) were used concomitantly if average normal renal and hepatic functions were present. One patient was treated by amputation below the knee, since it was feared that he could not withstand the shock of midthigh amputation. This instance suggests that the midthigh amputation in a patient with arteriosclerotic and diabetic gangrene of the toes may be supplanted by amputation at a site of election below the knee if dicumarol is administered. This thesis was supported in another patient, whose leg was amputated below the knee for diabetic gangrene of the toes.

California and Western Medicine, San Francisco

60:1-44 (Jan.) 1944

*Arthritis and Allied Conditions in an Army General Hospital. E. W. Boland.—p. 7.
Abdominal Trauma. R. B. McCarty.—p. 9.
Diabetes Mellitus: Some of Newer Factors in Its Etiology and Treatment. W. D. Sansum.—p. 13.
Poliomyelitis: Its Present Status. N. B. Nelson.—p. 18.
Obstructive Submucous Lipoma of Cecum. E. C. Moore.—p. 21.

Arthritis in an Army General Hospital.—Boland studied 350 cases of arthritis and allied conditions in the admissions to the medical service of an Army General Hospital. The cases were divided into those with peripheral joint complaints and those with symptoms referable to the back. The present discussion is limited to the first group, which comprised 61 per cent of the series. Approximately 19 per cent of the peripheral arthritides were of the rheumatoid type. Early joint effusion, particularly in the knees, has been common. In 70 per cent of cases the joint involvement has been confined to the lower extremities alone. The metatarsophalangeal and interphalangeal joints of the toes were involved in 41 per cent of cases, while the corresponding joints in the fingers were affected in only 10 per cent. Such a distribution in rheumatoid arthritis is in sharp contrast to that encountered in the general population. Bacteriologic identification of the gonococcus and good clinical judgment are necessary before a diagnosis of gonorrheal arthritis can be made in the Army. If initial smears have failed to demonstrate the gonococcus, the diagnosis of gonorrheal arthritis has not been made. Osteoarthritis, gout and some of the rarer forms of arthritis have differed in no way from those seen in civilian practice. Psychogenic manifestations occur with appalling frequency in soldiers. Emotional upsets may bring about or intensify symptoms of pain, stiffness and limitation of motion in the joints and muscles. Twenty and six-tenths per cent of the cases with peripheral joint complaints were regarded as instances of psychogenic rheumatism, and 3.7 per cent of those with pathologic joint changes had a definite psychoneurotic coloring. Nineteen and one-tenth per cent of the group with backache were considered psychogenic and 26.5 per cent of those with roentgenographic or objective physical abnormalities of the back had a definite psychogenic overlay. In the vast majority of cases various psychoneurotic symptoms, such as anxiety, irritability, fatigue, insomnia and mental depressions, were present.

Canadian Medical Association Journal, Montreal

50:103-198 (Feb.) 1944

Preventive Medicine in Rural Canada. A. F. Menzies.—p. 103.
Prosthetic Face Reconstruction. J. Gerrie.—p. 104.
Immobilization and Infrequent Dressings in Treatment of Wounds and Infections. G. A. Fleet and F. D. Ackman.—p. 109.
Sulfonamide Treatment of Wounds. W. Magner and M. O. O'Sullivan.—p. 118.
Aspects of Diseases in the Tropics. D. C. Bews.—p. 124.
Whooping Cough: Skin Tests. N. Silverthorne, D. T. Fraser and A. Brown.—p. 129.
Agglutinin Titers of Pooled Sera. D. G. Gemeroy.—p. 131.
Further Report on Canadian Red Cross Food Parcels for British Prisoners of War. F. F. Tisdall.—p. 135.
Observations on Commercial Bread as Source of B Vitamins. A. T. Owens and E. W. McHenry.—p. 138.
Acute Membranous Stomatitis and Conjunctivitis (Report of 3 Cases). J. A. Langille.—p. 141.
Use of Curare in Anesthesia and for Other Clinical Purposes. H. R. Griffith.—p. 144.
Anorectal Suppurative Disease and Anorectal Fistula. E. A. Daniels.—p. 147.
Training of Medical Officer. B. D. Robertson.—p. 154.

Gastroenterology, Baltimore

2:1-84 (Jan.) 1944

*Addisonian Pernicious Anemia Without Achlorhydria: Does It Exist? J. M. Askey.—p. 1.
Disease in Tropical War Zones: III. Diseases of Mediterranean Basin and of Tropical Africa. E. C. Faust.—p. 13.
Effect of Motion on Roentgenographic Appearance of Stomach and Small Bowel. F. E. McDonough and M. Schneider.—p. 32.
Pharmacologic and Clinical Study of Spasmolytic Drugs. H. Necheles, W. H. Olson, F. Neuwelt and E. Spier.—p. 46.
Life Cycle of Carcinoma of Stomach: Report of 3 Interesting Cases of Carcinoma of Pylorus. M. Feldman.—p. 60.

Pernicious Anemia Without Achlorhydria.—Askey shows that it is entirely contrary to the history of addisonian pernicious anemia to occur in the presence of gastric secretion of free hydrochloric acid. The precise diagnosis of addisonian pernicious anemia requires: 1. Elimination of the conditions other than addisonian pernicious anemia which may cause a loss of intrinsic factor. 2. A biologic assay showing absence of intrinsic factor. 3. A response to desiccated hog stomach, which furnishes ultimately the specific anti-pernicious anemia liver principle, or to a highly purified liver fraction, such as the Dakin-West fraction. These postulates, although rigid, are mandatory if pernicious anemia is to be diagnosed in an individual with acid present. The diagnosis not infrequently has been made and later proved to be wrong. Reports of 47 cases of pernicious anemia without achlorhydria by other observers are reviewed by the author. He shows that none of these have been proved by complete precise criteria to be addisonian pernicious anemia. It would seem wise to restrict the term pernicious anemia to the true or addisonian pernicious anemia characterized by absolute anacidity, loss of intrinsic factor

and reduction of the specific liver principle. Until precise critical tests have proved that acid secretion can persist in pernicious anemia, the presence of acid in any case must be considered as ruling out addisonian pernicious anemia. The existence of true pernicious anemia without anacidity as yet cannot be accepted.

Journal of Clinical Endocrinology, Springfield, Ill.

3:625-698 (Dec.) 1943

*Five Cases (3 in Siblings) of Idiopathic Hypoparathyroidism Associated with Moniliasis. A. Sutphin, F. Albright and D. J. McCune. —p. 625.
Parathyroid Tetany Treated with Massive Doses of Vitamin D. E. L. Sevringhaus and Ruth St. John.—p. 635.
Combined versus Independent Hydrolysis and Extraction of Urinary 17-Ketosteroids, with Special Reference to Choice of Solvents. H. B. Friedgood, E. H. Taylor and M. L. Wright.—p. 638.
Dysfunctional Uterine Bleeding. K. J. Karnaky.—p. 648.

Idiopathic Hypoparathyroidism with Moniliasis.—Sutphin and his associates describe the histories of 5 patients in whom idiopathic hypoparathyroidism was accompanied by moniliasis. The first 3 of the patients were siblings. The authors discuss the association of moniliasis with hypoparathyroidism from four different points of view: (1) that there is no connection, (2) that hypoparathyroidism might be the result of moniliasis, (3) that moniliasis might result from hypoparathyroidism and (4) that both conditions might result from a third factor. They reach no definite conclusion but point out that the time relationships in the case histories suggest that the moniliasis precedes the hypoparathyroidism. Since the father and mother of patients 1, 2 and 3 were first cousins, and since all 3 patients, the father and other siblings had congenital hypochromic polycythemia, the possibility exists that the susceptibilities to monilia infection and to hypoparathyroidism are both connected with some defect in the germ plasm. The nail changes resulting from moniliasis did not improve in case 1 when the serum calcium was restored to normal by dihydrotachysterol therapy; they are therefore not to be confused with the nail changes which are part of a generalized ectodermal disorder that accompanies certain cases of hypoparathyroidism and are relieved by specific therapy. Furthermore, the fact that the changes were confined to the fingernails and did not involve the toenails suggests an infectious as opposed to a metabolic etiology. With the Ellsworth-Howard test it was demonstrated that case 1 reacted normally to parathyroid injection; this rules out "pseudohypoparathyroidism." Attention is called to the previously reported association of papilledema and increased intracranial pressure with hypoparathyroidism; their combination in case 1 with jacksonian epilepsy led to the faulty diagnosis of brain tumor. The authors also point out that other observers have reported the histories of 2 siblings in both of whom moniliasis was associated with Addison's disease and in 1 of whom hypoparathyroidism was also present.

Journal Neuropath. and Exper. Neurology, Baltimore

3:1-100 (Jan.) 1944

Subependymal Cell Plate (Matrix) and Its Relationship to Brain Tumors of Ependymal Type. J. H. Globus and H. Kuhlenbeck. —p. 1.
*Infantile Toxoplasmic Encephalitis, Report of Case. G. Steiner and D. H. Kaump.—p. 36.
Spontaneous Striatal Degeneration in Monkey. R. Richter and H. Klüver.—p. 49.
Congenital Agyria and Defect of Corpus Callosum. H. Josephy. —p. 63.
Effects of Lesions of Periaqueductal Gray Matter on Macaca Mulatta. P. Bailey and E. W. Davis.—p. 69.
Syndrome of Anterior Spinal Artery of Medulla Oblongata. C. Davison.—p. 73.
Pathologic Changes in Brain After Electric Shock: Experimental Study on Dogs. W. L. Lidbeck, with technical assistance of Lurlene Green.—p. 81.
Behavior Disturbances Related to Decomposition of Reflex Activity Caused by Cerebral Injury: Experimental Study of Cat; Review. O. R. Langworthy.—p. 87.

Infantile Toxoplasmic Encephalitis.—The following characteristics are presented by toxoplasmic encephalitis in infants, according to Steiner and Kaump: The onset of symptoms is at birth or during the first weeks of infancy; convulsions and possibly other organic neurologic manifestations, internal hydrocephalus, chorioretinitis and cerebral calcifications are present which can be demonstrated by x-ray studies. The cerebrospinal fluid yields a high protein content, an increased cell count and occasional xanthochromia. Pathologically the disease is characterized by focal meningeal and cerebral inflammatory lesions, necrotic areas showing advanced calcification, miliary granulomas and the presence of the causative organism either singly or multiple in cysts. The toxoplasma is a parasite classified as a protozoon. The mode of transmission and the port of entry into the human body are not known. Pregnant women seem to transmit the disease to their offspring before birth without themselves acquiring clinical manifestations. The authors present a case of infantile toxoplasmic encephalitis. It was complicated by erythroblastosis fetalis. Toxoplasmic encephalitis in its severe form is essentially a disease of early infancy and appears to be acquired in late prenatal life. The immature brain of late prenatal and early postnatal life appears to be susceptible to toxoplasmic infection; the infantile meninges and brain appear to have a low resistance to toxoplasmas. The fully developed toxoplasmic cyst produces no reaction and no granuloma. When the cyst ruptures there is at first likewise no reaction. However, as the parasites begin to spread, formation of a granuloma begins. The final reaction to the free toxoplasmas is the fully developed granulomatous lesion. The diagnostic criteria in infantile toxoplasmic encephalitis include gross and microscopic pathologic changes, morphologic identification of the organism, the clinical picture, the isolation of the organism and the presence of immune bodies in the blood of the mother and the infant. The history and the gross and microscopic aspects of calcification, necrosis, inflammation, parasitic cysts and single parasites are of greatest importance in establishing a diagnosis.

Journal of Pediatrics, St. Louis

24:1-122 (Jan.) 1944

*Subdural Hematoma in Infancy. F. D. Ingraham and D. D. Matson. —p. 1.
Etiology of Congenital Cerebral Palsy: Statistical and Clinical Study. H. Yannet.—p. 38.
Clinical Modification of Whooping Cough by Use of Alum Precipitated Diphtheria Toxoid: Experimental and Clinical Studies. J. Muñoz Turnbull and G. Varela.—p. 46.
*Treatment of Epidemic Diarrheas and Dysenteries in Infants and Young Children: Comparative Study of Different Treatments and Their Results. K. Glaser and J. W. Bruce.—p. 53.
Problems in Management of Rheumatic Disease in Childhood. L. M. Taran.—p. 62.
Static and Dynamic Physical Fitness of Adolescents. J. R. Gallagher. —p. 81.
Effect of Rachitogenic Diets, Partial Inanition and Sex on Resistance of Cotton Rats to Virus of Poliomyelitis. H. M. Weaver, with technical assistance of Helen Ammon and Norma Hastings.—p. 88.

Subdural Hematoma in Infancy.—Ingraham and Matson present observations on 98 children with subdural hematoma, all of whom were treated under supervision of the neurosurgical service according to a uniform plan. This group includes only patients seen since 1937. Previous to 1937 only 2 or 3 patients a year with subdural hematoma were seen. The authors feel that the apparent rise in the incidence of the disease in their hospital population during the last six years is not a real one. Increased interest has led to a more diligent search for these patients, and the results have been gratifying. The authors stress that subdural hematoma is most frequently seen in the first six months of life. Trauma to the head is probably always a factor. There is no characteristic clinical picture. Generalized symptoms such as fever, vomiting, hyperirritability and failure to gain in weight are frequently found alone or in addition to the more specific neurologic findings of convulsions, stupor and paralysis. Infants who show early abnormal enlargement of the head should never be abandoned as having incurable hydrocephalus until subdural hematoma has been ruled out. The diagnosis can be made by bilateral puncture of the subdural space, the technic of which is described. The increase in brain volume during the first two years of life must be unrestricted to insure the normal mental development of a child. Therefore radical craniotomy with excision or wide decompression of constricting subdural membranes is essential if cerebral deficiency is to be avoided. Infants during the first two years of life will tolerate radical surgery well if proper preliminary measures and supportive treatment are undertaken. The therapy used at the Children's Hospital since 1937 is discussed. In all of the 98 children treated by the authors the diagnosis was made on the basis of subdural puncture. In 94 of these, bilateral

temporal burr holes were made. Sixty-two patients showed subdural membranes on one or both sides. Ninety-four craniotomies were performed, with an operative mortality of 5.3 per cent and a case mortality of 7.9 per cent. Of the 57 patients who have been adequately followed for periods of from 6 months up to 5 years of age, 23 per cent are retarded or grossly deficient and 77 per cent show normal behavior for their age. These results, it is felt, have sufficiently improved the outlook in subdural hematoma to call for a more diligent search for these infants. Whereas treatment is fundamentally a neurosurgical problem, suspicion of the diagnosis must rest primarily with the pediatrician and the general practitioner.

Treatment of Diarrheas and Dysenteries in Young Children.—Glaser and Bruce review observations on infants and children with epidemic diarrhea or dysentery who were treated in the Louisville General Hospital during July, August and September from 1938 to 1942, with special attention to the patients of 1942. They divide their patients into two groups, those with diarrheas and those with dysenteries. In the first group they placed all cases classified as nutritional diarrhea and those which were caused by parenteral infection. The second group contains all cases of "specific" diarrhea caused by organisms belonging to the dysentery group. Except for the isolation technic observed in dysentery and the different selection of sulfonamides, the authors have applied the same method of treatment in the two conditions. Rest is essential and was provided. During a period of starvation lasting twelve hours only water and medication were given. The prevention or treatment of dehydration is of greatest importance. By cup or bottle, water was offered at fifteen to thirty minute intervals. In cases of advanced dehydration or acidosis, fluid was given not only orally but also intravenously. By continuous drip through a fixed ankle vein cannula, a steady flow of isotonic solution of sodium chloride, 5 per cent dextrose in sterile water or one of the two Hartmann's solutions was given for the first thirty-six hours. After hydration has improved, blood transfusions are of value. When hemoconcentration is too high, plasma has been given. The nonspecific type of diarrhea was treated with sulfathiazole and the specific diarrhea with sulfaguanidine. Because of delayed diagnosis, however, some specific types were treated with sulfathiazole. Bismuth compounds and camphorated tincture of opium were used only in resistant cases. In 1 instance polyvalent dysentery antiserum was used with striking result. Beginning twelve hours after admission the infants are given as much milk as they will take. The amount is neither limited nor forced. The orders read "Buttermilk as tolerated," or "Skimmed boiled milk ad libitum." The authors found this method successful. It has decreased not only the length of hospitalization but also the death rate.

Journal Pharmacology & Exper. Therap., Baltimore

80:1-117 (Jan.) 1944. **Partial Index**

Vascular Fragility and Permeability as Influenced by Various Agents: I. Description of Experimental Method and of Effects of Various Substances Related to Vitamin P. G. J. Majovski, A. J. Lesser, H. C. Lawson, H. O. Carne and C. H. Thienes.—p. 1.
Studies on Physostigmine and Related Substances: I. Quantitative Relation Between Dosage of Physostigmine and Inhibition of Cholinesterase Activity in Blood Serum of Dogs. O. Krayer, A. Goldstein and F. L. Plachte.—p. 8.
Methemoglobinemia After Administration of p-Amino-Acetophenone and p-Aminopropiophenone. J. M. Vandenbelt, C. Pfeiffer, Margaret Kaiser and Margaret Sibert.—p. 31.
Pharmacologic Action of Erythrina Alkaloids. K. Unna, M. Kniazuk and J. G. Greslin.—p. 39.
Pharmacologic Study of Extract of Erythrina Crista Galli (Ceibo). R. Pichard and J. V. Luco.—p. 62.
Distribution of Radiant Energy in Fluorescent Spectra of Atabrine and Some Other Derivatives of Acridine. T. C. Butler.—p. 70.
Formation of Methemoglobin: III. Influence of Total Hemoglobin on Formation of Methemoglobin from Acetanilide. G. Lolli, D. Lester and Miriam Rubin.—p. 74.
*Detoxication of Neoarsphenamine by Means of Various Organic Acids. E. W. McChesney, O. W. Barlow and G. H. Klinck Jr.—p. 81.
Pharmacologic Basis for the Widely Varying Toxicity of Arsenicals. R. B. Hogan and H. Eagle.—p. 93.
Determination of Salicylic Acid in Plasma. B. B. Brodie, S. Udenfriend and A. F. Coburn.—p. 114.

Detoxication of Neoarsphenamine by Various Organic Acids.—McChesney and his collaborators made further studies on the detoxifying action of several organic acids, particularly ascorbic acid, on neoarsphenamine. They found that the toxicity of neoarsphenamine for albino rats is materially reduced by ascorbic, isoascorbic, *d*-glucoascorbic and *p*-aminobenzoic acids. The most favorable effect is obtained if the arsenical and protective agent are injected intravenously in the same solution, but the acids are somewhat effective if injected simultaneously at another site. The function of the ascorbic acids appears to be primarily that of preventing oxidation, chiefly after injection. The mechanism by which *p*-aminobenzoic acid reduces toxicity is obviously different. There is evidence that the therapeutic efficiency of some typical arsenicals is not altered by the detoxicants.

Journal of Urology, Baltimore

51:1-116 (Jan.) 1944. **Partial Index**

*Renal Cysts, Simple and Otherwise. W. F. Braasch and J. A. Hendrick.—p. 1.
Secondary Bacteriuria Associated with Renal Tuberculosis. R. W. Corbitt.—p. 11.
Postcaval Ureter. C. L. Wilson and J. Herzlich.—p. 14.
Ureterocele with Prolapse Through Urethra. J. L. Emmett and G. B. Logan.—p. 19.
Congenital Hourglass Bladder. J. Zellermayer and H. E. Carlson. —p. 24.
Lymphosarcoma of Urinary Bladder. N. P. Rathbun and H. L. Wehrbein.—p. 31.
Course of Prostatic Ducts and Anatomy, Chemical and X-Ray Diffraction Analysis of Prostatic Calculi. C. Huggins and R. S. Bear. —p. 37.
Calculi of Prostate Associated with Ochronosis and Alkaptonuria. H. H. Young.—p. 48.
Technic of Prostatic Biopsy. A. A. Roth and H. Turkel.—p. 66.
Determination of Blood Loss During Transurethral Resection. H. L. Kretschmer and E. F. Ockuly.—p. 69.
Cavernous Hemangioma of Testicle. R. P. Morehead and W. C. Thomas.—p. 72.
*Carcinoma of Spermatic Cord and Epididymis Extension from Primary Carcinoma of Stomach. L. G. Lewis, W. E. Goodwin and W. S. Randall.—p. 75.
Influence of Aniline Dyes on Urinary Tract Tumors. D. K. Rose. —p. 81.
Clinical Application of Urea Spot Test. M. Plotz, N. E. Reich and H. N. Naumann.—p. 85.
Recent Cases Illustrating Dangers of Sulfa Drugs. J. K. Ormond and R. B. Roth.—p. 92.
Sulfonamide Anuria. J. C. McClelland.—p. 97.
Combined Antimicrobial Activity of Urea and Sulfathiazole in Urine. E. R. Neter and Phyllis Clark.—p. 101.
Chemical Basis of Uremia: Blood Phenol. P. R. Roen.—p. 110.

Renal Cysts.—According to Braasch and Hendrick, renal cysts are formed by retention of renal secretion consequent to obstruction in the renal tubules. They assume clinical significance only when they become so large or so numerous as to cause renal dysfunction or when they become apparent on physical or urographic examination. The authors limit this discussion largely to the clinical data involving the so-called simple cyst. They show that the term solitary cyst applied to a renal cyst is a misnomer. Examination at operation or at necropsy usually reveals other small cysts in one or both kidneys. Urography, either excretory or retrograde, offers the simplest form of diagnosis. The excretory urogram will offer sufficient diagnostic data in many cases, but greater accuracy usually is obtained by the retrograde urogram. The differentiation of urographic deformity caused by renal cyst from that caused by renal neoplasm may be exceedingly difficult and is a frequent cause of diagnostic error. In most cases surgical exploration will be advisable in order to establish an accurate diagnosis. Multiple simple cysts may be confused on surgical exploration with polycystic disease. Multilocular cysts differ from the ordinary type of multiple simple cyst in that a single large cyst is subdivided into smaller segments. Peripelvic (pyelogenic) cysts are differentiated from simple renal cysts in causation, clinical course and treatment. Cystic hypernephroma occasionally may be confused with simple cyst, both on clinical and on casual surgical examination. Hypertension seldom is caused by simple cysts. The frequent incidence of hypertension in cases of polycystic disease is in contrast. Aspiration of cysts as a diagnostic procedure occasionally may be indicated in cases in which surgical exploration is inadvisable. The procedure, however, may be unsatisfactory because of possible error of diagnosis and complications which may follow it. Surgical exploration usually is more satisfactory than aspiration, and surgical excision of the cyst is a better treatment.

Carcinoma of Spermatic Cord and Epididymis Extension from Carcinoma of Stomach.—Lewis and his associates present the history of a 19 year old private in whom a swelling in the right scrotum was the presenting symptom. The diag-

nosis was at first obscure, as the early appearance of the scrotal mass overshadowed the relatively minimal gastrointestinal symptoms. Removal of the scrotal mass disclosed an anaplastic carcinoma. The patient died about six weeks later, and necropsy disclosed primary carcinoma of the stomach with extension by direct peritoneal implant down both inguinal canals involving the cords on both sides and the epididymis on the right side. The family history revealed that the father and a paternal uncle both had died of cancer at an early age. This stresses the importance of familial tendency in cancer. This is only the fourth report of the extension of an intra-abdominal tumor to the spermatic cord and epididymis. This case emphasizes to the urologist the importance of looking further afield in obscure cases of testicular disease.

Laryngoscope, St. Louis

54:1-54 (Jan.) 1944

Chondroma of Larynx: Review of Literature and Report of 2 Cases. J. W. McCall, S. M. Dupertuis and F. S. Gardiner.—p. 1.
Nasoalveolar Cysts. F. A. Sooy.—p. 18.
Training for Optimum Use of Hearing Aids. S. R. Silverman.—p. 29.
Review of Articles on Tuberculosis in Field of Otolaryngology Chiefly for Late 1942 and Early 1943. F. R. Spencer.—p. 37.

Military Surgeon, Washington, D. C.

94:65-130 (Feb.) 1944

Burns Incident to War: Measures for Their Prevention and for Treatment. L. H. Roddis.—p. 65.
Teamwork on Health Front. T. Parran.—p. 76.
Air Evacuation. D. N. W. Grant.—p. 80.
Veterans' Problems of Present War. F. T. Hines.—p. 82.
Preventive Medicine at Front. J. S. Simmons.—p. 85.
Today and Tomorrow in Aviation Medicine. W. S. Jensen.—p. 89.
War Dentistry. J. C. Brauer.—p. 93.
Use of Medical Service of Fixed Hospital in Air Attack on Oahu, Hawaiian Islands, Dec. 7, 1941. F. E. Weatherby.—p. 95.
Amphibious Operations. D. S. Knowlton.—p. 96.
The Shipwrecked. P. H. Futcher.—p. 100.
Cases Rejected for Army Service on Basis of Chest Films Alone. W. D. Wise.—p. 103.
Predetermining Dental Survey. S. L. Beckwith-Ewell.—p. 104.
Acute Meningococcemia. B. M. Schwartz, J. T. Thornton Jr. and C. J. Lundy.—p. 105.
*Rapid Detection of Sugar in Urine: Using a Modified Bismuth Oxychloride Spot Test. F. P. Guidotti and J. H. Winer.—p. 111.

Rapid Detection of Sugar in Urine.—Guidotti and Winer point out that Mattice suggested the dry hydroscopic bismuth oxychloride powder mixture (galatest), having used it successfully for screening out the "negatives" in a diabetic clinic. To determine the accuracy of this test, comparative series of 15,000 urine specimens were studied using the bismuth powder and Benedict's test simultaneously. The powder test proved valuable. Small heaps of dry powder are placed in rows on white paper and are pressed down lightly with the bottom of the vial. One small drop of urine is deposited on the powder. When positive, the white powder turns gray or black instantly. In the comparative tests the urine was simultaneously added to the preheated Benedict's solution. The powder does not give a satisfactory quantitative estimation; therefore Benedict's test is necessary for rechecks, which are performed when sugar is found. The authors conclude that the accuracy, reliability and speed of mass urinalysis are enhanced by the use of a dry bismuth oxychloride mixture for spot test examination for sugar.

New England Journal of Medicine, Boston

230:63-94 (Jan. 20) 1944

Refrigeration in Surgery of Extremities. P. R. Hinchey.—p. 63.
*Eruptive Fever Involving Mouth and Eyes (Stevens-Johnson's Disease): Report of Case. R. C. Murphy Jr.—p. 69.
Pulmonary Actinomycosis: Treatment with Sulfonamides. N. R. Pillsbury and J. D. Wassersug.—p. 72.
Abdominal Surgery. A. W. Allen.—p. 74.

Eruptive Fever Involving Mouth and Eyes.—Murphy reports that a man aged 22 was hospitalized three days after he had noticed a swelling between the upper lip and the gum. Later blisters began to appear on the buccal mucous membrane. At the time of hospitalization he had a temperature of 101 F. The conjunctivas were diffusely inflamed. The buccal mucous membrane, gums, palate and uvula were covered with many tight vesicles. There was also a small amount of red inflammatory reaction and sticky exudate about the urethral meatus. During the first two days of hospitalization the disease ran an alarming, fulminating course. The temperature rose rapidly and ran a hectic course, up to 104.6 F. All the pearl-like vesicles in the mouth ruptured, leaving a loose, dirty, whitish slough. By the third day there was a massive slough involving the entire mucous membrane of the mouth and sparing only the tongue. The nasal mucous membrane sloughed in a less dramatic manner. Large blebs appeared on the glans penis also with superficial sloughs. Both conjunctivas were inflamed, but no vesicles formed about the eyes. A semipurulent exudate flowed continually from the eyes. On the arms and legs punctate red areas appeared and expanded, and in the center of each a vesicle appeared. These vesicles ripened into thin walled bullas and ruptured. On the fifth day the temperature fell and the patient began to improve. The sloughs in the mouth and on the penis were not complete before the third week. A conjunctival culture yielded Staphylococcus aureus. Smears of the bullas were negative both for eosinophilic polymorphonuclear leukocytes and for organisms. No significant evidence of the heavy metals was found on qualitative tests of two twenty-four hour urine specimens. The patient had had a mercury-amalgam tooth filling one and one-half months previously, but no other significant metal or drug history could be elicited. The therapeutic measures included sulfadiazine for five days, the forcing of fluids, colonic irrigations, calcium gluconate intravenously and salves, washes and other local applications to the mouth, penis and eyes. At the end of seventeen days the skin lesions had crusted and mostly fallen away. The author says that nothing is known of the fundamental nature of the disease or of its etiology. Neither drugs nor Vincent's organisms have been implicated. The disease is not typical of erythema multiforme, and it is the enanthem rather than the exanthem that is its constant feature.

Pennsylvania Medical Journal, Harrisburg

47:417-544 (Feb.) 1944

Complications of Acute Mastoiditis. R. L. Moorhead.—p. 431.
Panel Presentation on Art and Science of Therapeutics. A. H. Aaron. —p. 440.
Use and Abuse of Sulfonamides in Surgery. C. M. Smyth Jr.—p. 446.
Use and Abuse of Sulfonamides in General Practice. H. A. Reimann. —p. 448.
Use and Abuse of Barbiturates. H. B. Gardner.—p. 451.
Primary Carcinoma of Lung: Review of 30 Proved Cases. L. M. J. Freedman, H. W. Jacox and R. G. Alley.—p. 455.
Physiology of Nose and Its Bearing on Treatment. D. S. DeStio. —p. 461.
Industrial Injuries to Fingers. J. J. Toland Jr. and I. H. Kornblueh.—p. 466.
Obstetric Deaths in 1942 (Philadelphia) Resulting from Operative Delivery Other Than Cesarean Section. J. M. Alesbury.—p. 474.
Comparison of Results of Intracapsular and Extracapsular Cataract Extraction. H. C. Fulton.—p. 478.
Pediatrician's Role in Speech Correction. E. L. Piper.—p. 483.
Pelvic Myofibromas of Extrauterine Origin. C. G. Strickland.—p. 489.

Virginia Medical Monthly, Richmond

71:57-112 (Feb.) 1944

Red Cross Activities at Home and Abroad. B. M. Jones.—p. 59.
Penicillin in Treatment of Osteomyelitis and Other Infections: Case Report. M. A. Pittman.—p. 66.
Prevention of Tetanus. J. H. Lyons.—p. 71.
Newer Treatments in Neuropsychiatry. Beverley R. Tucker.—p. 75.
Kenny Treatment for Infantile Paralysis: Year's Observation of 6 Cases. C. J. Frankel.—p. 79.
Medicine Under Czars and Under Stalin. J. Krimsky.—p. 84.
Physician's Responsibility and Relation to Community. C. L. Harrell.—p. 88.
Breeding Better People for Peace: Human Nature Can Be Changed. J. S. Horsley.—p. 93.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

52:41-86 (Feb.) 1944

Recovery of Primate Eggs and Embryos: Methods and Data on the Time of Ovulation. C. G. Hartman.—p. 41.
Physiologic Intermenstrual Bleeding—Gross or Microscopic—As a Possible Diagnostic Aid in Abdominal Pain Studies. R. N. Rutherford.—p. 62.
Duodenal Obstruction and Stasis. M. S. Rosenblatt.—p. 69.
Idiopathic Spontaneous Pneumothorax. S. H. Babington.—p. 73.
Recent Advances in Allergy. P. Schonwald.—p. 77.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

55:289-324 (Dec.) 1943

Familial Xanthomatosis. J. C. Swanson.—p. 289.
Note on Case of Blastomycosis Cured by Sulfapyridine and Sulfathiazole. M. Albert.—p. 294.
Naevus Acneiformis Unilateralis. E. L. Cohen.—p. 297.

Journal of Physiology, Cambridge

102:259-372 (Dec. 31) 1943. **Partial Index**

Effect of Barbiturates on Serum Cholinesterase. F. Schütz.—p. 259.
Antagonism Between Posterior Pituitary Lobe and Insulin. L. Wislicki. —p. 274.
Influence of Sympathetic Nervous System on Capillary Permeability in Traumatic Shock. D. Engel.—p. 281.
Blood Volume of Normal Animals. F. C. Courtice.—p. 290.
Differentiation in Absorption of Olive Oil and Oleic Acid in Rat. A. C. Frazer.—p. 306.
Some Experiments on Possible Relationship Between Vitamin C and Calcification. G. H. Bourne.—p. 319.
Lipolysis and Fat Absorption. A. C. Frazer.—p. 329.
Output of Cortical Hormone by Mammalian Suprarenal. Marthe Vogt. —p. 341.
Metabolism of Phosphate and Carbohydrate in Extracts of Human Muscle and Brain. G. D. Greville and H. Lehmann.—p. 357.
Alkali in Pancreatic Secretion. C. O. Oldfelt.—p. 362.

Lancet, London

1:39-72 (Jan. 8) 1944

*Sulfonamide Dermatitis: Sensitization from Local Application. B. C. Tate and I. Klorfajn.—p. 39.
Gunshot Wounds of Fronto-Orbital Region.—p. 44.
*Tender Muscles in Sciatica: Electromyographic Studies. F. A. Elliott. —p. 47.
Phemeride: New Antiseptic Detergent. C. N. Hand.—p. 49.
Deposit in Seitz-Filtered Serum. G. E. C. Francis, G. A. Harrison and L. E. R. Picken.—p. 51.
Convulsions Under Anesthesia Treated by Change of Posture. A. Smith. —p. 52.

Sulfonamide Dermatitis from Local Application.—Tate and Klorfajn report that 55 of a total of 2,280 admissions to the skin department of a military hospital were cases of sulfonamide dermatitis produced by local applications of these drugs. After a period of sulfonamide application to some skin disease or minor injury an irritating dermatitis appeared. At first it was confined to the area under treatment ("primary eruption") and in 2 cases it remained so localized; but, in the rest, other regions, to which no sulfonamide had been applied, became affected ("secondary eruption"). The secondary eruption usually had the distribution commonly seen in sensitization to other chemicals, but in 4 cases it was strictly limited to areas exposed to light, and in 2 others, though covered areas were affected, it was especially severe on the exposed parts. The dermatitis was always eczematous, i. e. an inflammatory reaction with edema of the skin and innumerable intraepidermic vesicles scattered throughout the affected area. Some cases presented a more or less generalized weeping eczema; but the severity varied, depending largely on the length of time sulfonamide therapy was continued after sensitization had been established. Constitutional symptoms were commensurate with the severity of the eruption. Sulfanilamide had been used in most cases, but in 3 sulfapyridine appeared to be the offender. The diagnosis was suggested by the history, character and distribution of the eruption and was confirmed by patch tests and oral administration of sulfonamides. Patients sensitized to one of the sulfonamide drugs are thereafter sensitive to other members of the group. Sensitization may be so intense as to preclude subsequent administration of these drugs for other diseases. The authors conclude that topical sulfonamide therapy for skin diseases and minor injuries is unjustifiable. It should be reserved for cases in which withholding it might endanger life or lead to deformity.

Tender Muscles in Sciatica.—Elliott records observations on the tender spots, sometimes described as nodules, found in the muscles of the buttock and calf in certain cases of sciatica. They commonly occur in muscles with an extensor function, are sharply localized and, when palpated, give rise to pain, which may radiate down the limb. Both the local tenderness and the sciatica itself can in some cases be abolished by injecting procaine into the tender spots. Contemporary writers believe that these tender spots are the site of an inflammatory or rheumatic process which gives rise to referred sciatic pain and that the successful exhibition of procaine confirms the diagnosis and excludes other causes. It is not generally recognized that tender spots indistinguishable from the more benign forms of myalgia may be found in the muscles supplied by an irritated nerve root. This is most commonly encountered in sciatica as the result of prolapse of the nucleus pulposus but also occurs in spinal tumors. The author demonstrates this on the basis of 2 case histories. Since the tender spots are confined to the muscles innervated by the affected root and disappear when the source of irritation is removed by operation, an inflammatory origin can be excluded. Use was made of the fact that contracting muscle gives rise to action potentials which can be recorded by an electromyograph. A table shows observations on 14 cases of sciatica in which a prolapsed disk was found at operation. In 8 cases there was local tenderness and in 6 controls there was none. The insertion of the needle electrode into normal muscle evoked a momentary contraction of a few fibers. In the case of tender muscles this initial contraction affects more fibers and may be sustained for a second or two; i. e., the irritability is increased, and deep palpation of the surrounding muscle gives rise to fresh bursts of motor activity. The increase is limited to the tender areas of muscle and has been found in almost every case of deep tenderness. The author considers how these irritable foci can arise. The spasm is thought to be the source of pain and tenderness. Similar activity has been recorded in "fibrositis" of the shoulder girdle and in the extensor muscles of the arm and forearm in cases of "brachial neuritis" both with and without root signs. Muscle spasm is consequently considered to play a part in what may for convenience be called the rheumatic myalgias as well as in the less common root syndromes.

Medical Journal of Australia, Sydney

2:473-488 (Dec. 11) 1943

Shift to Higher Age Levels in Australia and United States: Its Sociological and Medical Interest. C. V. Crockett.—p. 473.
*Temperature in Shock: I. Local Effects. J. Devine.—p. 476.
Isolation of Pleuropneumonia-like Organisms from the Male Urethra. W. I. B. Beveridge.—p. 479.

Temperature in Shock.—It was Devine's impression that among the casualties in the hospital at Tobruk those who had been for some hours in the sea, in the cold of the Mediterranean winter, arrived at the hospital in good general condition, even though they had extensive burns and wounds, and that they appeared to be in better condition than those who came from the surrounding land areas. These men had all been chilled generally as well as locally. The author decided to investigate whether the local application of a moderate degree of cold would decrease the local loss of plasma following shock-producing trauma. He describes experiments on 9 dogs in which a leg was subjected to trauma by blows with a mallet after a tourniquet had been put on. Then, with the tourniquet still in position, the leg was placed in a water bath at 50 C. for twenty minutes. This procedure had been found to produce shock when the tourniquet was released. When the tourniquet was released, the water was kept at 50 C. in 3 of the dogs, and in that of 3 others it was kept at about 8 C. The carotid blood pressure was continuously recorded, and every ten minutes the limb volume was recorded. The local increase in limb volume of those limbs kept at an average temperature of 52 C. was over three times that of limbs kept at an average temperature of 8 C. Only one dog whose leg was kept in a warm bath was alive at the end of one hundred minutes following the release of the tourniquet. The clinical application of the reported experimental work is that, first, heat should not be applied in the neighborhood of injuries that are likely to cause shock, for if this is done local loss of circulating fluid to the tissues will be increased; second, cooling of a traumatized limb may be effective in lessening the local loss of fluid from the circulation and may thus, in the light of experimental work published by others, be helpful in modifying the onset of shock.

Book Notices

The Techniques of Self-Help in Psychiatric After-Care Developed by Recovery, Inc., the Association of Former Mental Patients. Volume I: Recovery's Self-Help Techniques, History and Description. By Abraham A. Low, M.D., Founder and President of Recovery, Inc. Paper. Price, $1.25. Pp. 136. Chicago: Recovery, Inc., 1943.

The Techniques of Self-Help in Psychiatric After-Care Developed by Recovery, Inc., the Association of Former Mental Patients. Volume II: Group Psychotherapy: A Record of Class Interviews with Patients Suffering from Mental and Nervous Ailments. By Abraham A. Low, M.D., Founder and President of Recovery, Inc. Paper. Price, $1.25. Pp. 88. Chicago: Recovery, Inc., 1943.

The Techniques of Self-Help in Psychiatric After-Care Developed by Recovery, Inc., the Association of Former Mental Patients. Volume III: Lectures to Relatives of Former Patients. By Abraham A. Low, M.D., Founder and President of Recovery, Inc. Paper. Price, $1.25. Pp. 125. Chicago: Recovery, Inc., 1943.

The three books under discussion are not separate treatises but are continuations of one another and deal in the main with two problems: group psychotherapy and the mental hygiene care of patients after discharge from mental hospitals. Since the first world war psychiatry may be said to have passed from the strictly symptomatic and custodial type of treatment of mental illness and is attempting something by way of effective psychotherapy. From the standpoint of such treatment the problem forever confronting the psychiatric hospital is the small size of the staff that can devote its full time to psychotherapy as compared with the very large number of patients who need such treatment. The most effective form of psychotherapy so far devised is psychoanalysis, but it is based primarily on a very intimate personal relationship of the psychotherapist to the patient, so that with one patient being handled at one time the total number of patients that can be so handled must of necessity be very small. While the few patients under such care profit a great deal by the therapy, the rest remain untreated. For this reason there have been from time to time attempts on the part of psychiatrists to circumvent this rather luxurious form of treatment and devise means whereby a large number can be treated with sufficient effectiveness to make it worth while.

In 1920 Dr. Edward Lazell, then at St. Elizabeths Hospital, Washington, D. C., attempted psychotherapy by discussing general psychotherapeutic problems before a group of patients. Later on Dr. Louis Wender, then at Hastings Hospital, New York, did quite effective work in group psychotherapy, of which he has published reports. At about the same time Schilder made like attempts at Bellevue. It is this type of work that Professor Low has been doing since 1937. It is realized, of course, even by those not necessarily committed to the psychoanalytic approach, that, at best, group psychotherapy can be effective only at a superficial level and can never reach the depths at which the basic conflicts are formed. The reason for this is that the most intimate aspects of a person's life could hardly be revealed in the presence of others, for such presence acts as an inhibitor for fuller catharsis. Withal, and in spite of its limitations, group psychotherapy is a decidedly profitable endeavor if one only bears in mind that it is not basic and final. It can no doubt reach a certain type of patient who needs but little push to start him on the road to recovery. To other patients it can provide partial insight that may help them to be discharged as improved or socially recovered—not complete cures to be sure, yet sufficient to help toward rehabilitation.

The brochure dealing with group psychotherapy is written in a fine and fluent style and can be easily understood by any one with only a high school education. The other two brochures take up a problem primarily of patients who have already recovered. This is really an extension of mental hygiene work; a type of extramural psychiatry, however, which has been practiced but little. It attempts a follow-up of patients who have been confined by an illness to a psychiatric institution. Many of the discussions are reprints of articles published in a previously published medium, "Lost and Found Journal," which accounts for a great deal of repetition; yet one does not object to these so much because these repetitions really tend to emphasize the problem. This "after hospital care" helps to reduce the number of relapses which often come from the social isolation due, in turn, to the stigma that is as yet attached to the problem of mental illness. It must be a pleasure and satisfaction to see the many men and women coming together without a consciousness of stigma and embarrassment. Admittedly, this "recovery self-help project" has not entirely eradicated the stigma connected with mental disease, but certainly it has robbed it of a good deal of its malignant force. The remark made by others may hurt the past patient and may even make him feel unhappy, but it does not make him feel guilty and certainly not abnormal.

In the third booklet, "Helpful and Healthy Advice," the same is given to relatives of former patients—what are the best things they can do to steer the patient toward complete mental health. It is attractively and delightfully written.

In all, these three booklets represent a real advance in our understanding and treatment of psychiatric problems. The reviewer wishes they could be reprinted in quantities of thousands, distributed to relatives of patients after the patients have been discharged or, for that matter, before discharge. It would go a long way toward the better management of mental illness and remove what prejudice and stigma still exist in the public mind.

Clinical Audiometry. By C. C. Bunch, M.A., Ph.D., Associate in Research Otology, Johns Hopkins University, Baltimore. Cloth. Price, $4. Pp. 186, with 74 illustrations. St. Louis: C. V. Mosby Company, 1943.

This volume is packed with significant advice on the practical aspects of testing hearing of a patient, whether an adult or a child. Particular attention, as the title indicates, is given to the use of the audiometer. The book contains a historical account of testing hearing by the tuning fork and the development of the modern audiometer. Being a codesigner of an audiometer, the author recorded a complete account of early experimentation in the field. He had a wide experience with audiometers in clinical applications, and the technic described in chapter III necessarily carries much weight. There are chapters on conductive and perceptive types of deafness and on the value of residual hearing.

The author devoted a chapter to the controversial field of selecting a hearing aid with the use of an audiometer. He assumes that the audiometer is of value for this purpose, but to the question "Can an otologist send an audiogram to a manufacturer with the assurance that a hearing aid will be selected to compensate for the losses shown in that audiogram?" he answered in the negative. He summed up by stating that in the final analysis the ability to hear and understand speech in a familiar language is the real test of a hearing aid.

Valuable advice is given on the construction of the soundproof room for use in audiometry. Since the author had considerable experience regarding the building of quiet rooms, this chapter is extremely interesting.

This book by the late Dr. Bunch deserves a place in all libraries of physicians who treat the ear.

La novela de las vitaminas. Por el Dr. Arturo León López. Con un prólogo del Profesor Doctor Pedro Escudero. Cloth. Price, $12.—m/arg. Pp. 449, with illustrations. Buenos Aires: Orientación Integral Humana Soc. de Resp. Ltda., 1943.

In this unusually well bound and illustrated book is presented the story of the discovery and development of the vitamins now recognized as having definite functions in the animal and human body. The romanticism surrounding the early interest in many of the vitamins is woven into their stories, thereby enhancing the appeal of the book for popular reading. The author makes generous use of pictorial sketches to demonstrate a close family relationship of certain vitamins or to depict the selective effects of given vitamins on various organs or systems of the body. In some cases the impression given by these diagrams implies more than the facts warrant. Another attractive feature is the inclusion of halftone portraits of scientists credited with being the pioneers in the various vitamin fields.

The statements throughout the book appear to be based on scientific fact and are so artfully woven into the stories of the vitamins that they make pleasant reading. As an additional contribution the author makes sound recommendations as to the value of hygiene and good food. Lists are given of foods which are known to contain particularly significant amounts of the

various vitamins as well as selected dietary lists which provide the known daily requirements for the numerous age groups and energy expenditures represented. Because of the attractive way in which the book presents a great deal of factual information, it makes a real contribution to popular knowledge of nutrition.

Forsdike's Textbook of Gynæcology. Revised, Enlarged and in Part Re-Written by J. H. Peel, M.A., B.M., B.Ch., Assistant Obstetric and Gynæcological Surgeon, King's College Hospital, London. Cloth. Price, $5.75; 21s. Pp. 440, with 216 Illustrations. New York: Grune & Stratton, Inc.; London: William Heinemann, Ltd., 1943.

Peel states that he has radically revised Forsdike's book. The present one has both good and bad points. The drawings are excellent. The photomicrographs and some of the photographs are poor. The chapter on the anatomy of the female reproductive organs is excellent. It is pleasing to see a discussion of puberty, menstruation, the menopause and the climacteric. The chapter on retrodisplacement and prolapse also are well written. However, there is no need for photographs of pessaries, especially those with harness to hold up the uterus. Photographs of various instruments, such as volsella and curets, should have been omitted. Under specific infections only gonorrhea, syphilis and chancroid are discussed; three pages are devoted to tuberculosis of the reproductive tract. A chapter on chronic metritis and diffuse hypertrophy of the uterus is well written and should form part of every gynecologic textbook. Discussion of abortion, hydatidiform mole and chorioepithelioma could be questioned in a gynecologic textbook. Chorioepithelioma is so rare that three and a half pages and two photographs should not have been devoted to it. The section on symptoms seems to be a "catch-all" for various complaints, such as vaginal bleeding, discharge, dyspareunia and urinary tract disease. The author is apparently an excellent clinician, but he advocates the use of more female hormones than are usually found in a textbook. The chapters on gynecologic operations are too brief, are not well illustrated and should have been omitted. In future editions the author should not mix the English and the metric system. The reviewer believes that there are other gynecologic textbooks which would be of more value to both student and physician than this one.

The Care of Tuberculosis in the Home. By James Maxwell, M.D., F.R.C.P., Assistant Physician and Demonstrator of Practical Medicine, St. Bartholomew's Hospital, London. Cloth. Price, 7s. 6d. Pp. 105, with 6 illustrations. London: Hodder & Stoughton, Ltd., 1943.

The author calls attention to many tuberculous patients who must be treated in the home before they can be admitted to sanatoriums and after they have been discharged from institutions, and also to a definite group who do not require sanatorium care. The book is written in such a way as to give the patient and members of the family information concerning the nature of the disease as well as its treatment and prevention. Emphasis is placed on contagion. The usual symptoms, such as pleurisy and hemoptysis, are discussed as well as the various methods of treatment. All the modern phases of tuberculosis work are presented in a general way. The last chapter is devoted entirely to prevention, and the author points out how the complete control of tuberculosis in England could be achieved without much difficulty and in a comparatively short time. This is true of any nation. Although there are statements in the book with which one might take exception, such as that pertaining to heredity, they are all of a minor nature, and the more important phases of tuberculosis work are presented in such a manner that one can recommend the book without qualification.

Patología digestiva del niño: Las diarreas, los teteros. Por el Doctor Guillermo Araoz Fraser, médico de la Gota de Leche "Andrés Bermúdez" de Chapinero, Bogotá. Paper. Pp. 226. Bogotá: Editorial Minerva, S. A., 1941.

As the author states, this book is written for the nonspecialized physician practicing urban or rural medicine in Colombia and being confronted every day with the manifold problems of infantile diarrheas in poor social surroundings. The author has achieved his purpose because his book reads easily, is highly practical and yet gives scientific background for a clearer understanding of the different clinical pictures. No doubt a useful book!

Scabies. By Kenneth Mellanby, B.A., Ph.D. Oxford War Manuals. General Editor: The Rt. Hon. Lord Horder, G.C.V.O. Cloth. Price $1.50. Pp. 81, with 10 illustrations. New York & London: Oxford University Press, 1943.

In this pocket size manual Mellanby records his observations on several hundred cases of scabies observed in Great Britain, where the disease has become common during the war. He found that it was more prevalent among civilians than among service men and that physicians both military and civilian made at least a 25 per cent error in their diagnoses of the disease. The itching in scabies is apparently the result of a true sensitization, and volunteer patients were seen to harbor the organism for as long as two months before the development of symptoms. This fact may possibly explain the "misconception" that the disease is spread by bedding, communal towels, money, lavatory seats and ordinary social contacts. Rather it is prolonged intimate contact that accounts for the spread of the disease, and "indeed disinfestation of clothing and bedding may reasonably be dispensed with." Treatment with sulfur ointments and benzyl benzoate preparations afforded the best results, and the latter is to be preferred because it is cleaner and to save fats. This handy volume considers also the anatomy and life history of the itch mite, the parasitology, the clinical picture of the disease, the differential diagnosis and the complications; and it is written in an interesting conversational manner.

Tuberculinothérapie dans certaines affections essentielles (investigation clinique). Volume II: Ozene. Por el Dr. Carlos Charlin C., professeur à la Faculté de médecine, Buenos Aires. [Including] Tuberculinothérapie dans les névralgies faciales idiopathiques, Fascicule II, Volume I. Paper. Pp. 264; 265-331, with illustrations. Santiago, Chile: Publications de l'Université du Chile, 1943.

This book is the second of a series of volumes on tuberculin therapy. The first was published in 1940 under the title La tuberculinothérapie dans les nevralgies faciales idiopathiques et certaines affections essentielles. Volumes III and IV, now in preparation, are concerned with tuberculin treatment of tuberculosis of the eye and chronic rheumatism. This volume, II, deals largely with treatment of ozene. However, the author devotes chapter 1 largely to the primary tuberculosis complex, the development of which he describes in considerable detail. He presents numerous illustrations, particularly photographs, of patients before and after tuberculin therapy. He reports numerous cases in considerable detail to show the benefit derived from tuberculin therapy in a number of conditions. Unquestionably Dr. Charlin and his collaborators have made the most comprehensive study of tuberculin therapy that has ever been done, and their results are such as to lead one to believe that this kind of treatment may have a great deal of value in numerous extrapulmonary conditions.

Personality and the Behavior Disorders: A Handbook Based on Experimental and Clinical Research. Edited by J. McV. Hunt, Assistant Professor of Psychology, Brown University, Providence, Rhode Island. Volumes I and II. Cloth. Price, $10 per set. Pp. 618; 619-1242, with illustrations. New York: Ronald Press Company, 1944.

This is an authoritative compendium of reviews of our present knowledge of personality structure and function. Each of the thirty-five chapters has been written by an expert in one or more of the biologic, experimental, psychologic, sociologic and psychiatric fields of personality study. The reviews are comprehensive, judicious and well documented, so that differences of interpretation and theory among the various contributors (as well as intriguing variations in point of view, vocabulary and literary style) can be fairly and profitably evaluated by the reader. The work has been expertly organized and edited, and the complete bibliographies and indexes make it an encyclopedic source of ready reference. These books deserve a place in the library of every psychiatrist, psychologist and sociologist; moreover, they will be welcomed by many a physician interested in modern scientific approaches to the normal or abnormal behavior of his friends and patients.

Selected Papers from the Royal Cancer Hospital (Free) and the Chester Beatty Research Institute. Volume II. Published by Order of the Governors of the Royal Cancer Hospital (Free) London. Boards. Price, 10s. Pp. 413, with illustrations. London, 1939-1940.

This book contains reprints of some thirty articles in medical periodicals on various phases of cancer, most of them published in 1939 and 1940.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

EFFECT OF SULFONAMIDES ON MASTOIDITIS AND OTITIS

To the Editor:—**There seems to be a good deal of controversy as to the advisability of using sulfonamides in otitis media and in early or suspected mastoiditis. What is the danger of masking a mastoiditis? If used, should sulfonamides be given only for a brief period and then be discontinued in order that spread of infection might be detected by flare-up of signs and symptoms? Is it conceivable that sulfonamides can be helpful in clearing up a mastoiditis aside from their action in preventing septicemia? Has the incidence of mastoiditis been affected by the advent of the sulfonamides?**

M.D., New York.

[This question was submitted to two consultants, whose respective replies follow.—ED.]

ANSWER.—Acute mastoiditis consists of a suppurative process within the system of air cells connecting with the middle ear cavity. The infecting organisms are usually of the types susceptible to the action of sulfonamides. These drugs have a bacteriostatic action throughout living tissue, including the lining of the mastoid cells. By inhibiting regeneration of bacteria they help control the infection. Discharge is thereby reduced and the existing pathway of drainage through the middle ear relatively more adequate. Experience has shown that sulfonamide therapy is more effective in the invasive stage, best results being obtained by administration of quantities sufficient to produce an adequate blood concentration within the first few hours, maintaining this concentration for three to six days, depending on the severity of the infection. Adequate fluid intake and output and careful observation for toxic effects are essential. When sulfonamide therapy has been given early and in adequate blood concentration the incidence of surgical mastoiditis has been materially decreased.

Sulfonamides have proved generally ineffective in sterilizing an abscess cavity. The infection may be kept localized, but drainage is usually necessary to effect a cure. The mastoid consists of a system of air cells, which in the presence of suppuration contain varying quantities of free pus, a condition which is not conducive to the most effective action of sulfonamides. If drainage is greatly impeded or cell breakdown has occurred, the drugs are less likely to effect a cure without surgical drainage. Symptoms and signs may be decreased or disappear, only to reappear on the stopping of drug therapy. This has been called "masking." This so-called masking represents the localizing effect of the drug on the infectious process and is desirable for its protective value to the patient. Surgical indications are, however, less easily evaluated. In general, experience has shown that when surgical indications are already present the safest procedure is chemotherapy followed by surgery. When surgical indications become evident either during or on cessation of chemotherapy, surgery should be promptly carried out, the chemotherapy being maintained or resumed for its protective value.

ANSWER.—The sulfonamides appear to have had a definitely beneficial effect in acute otitis media, not only in shortening the duration of the infection, but in decreasing the incidence of surgical mastoiditis and the other complications. The so-called masking effect is due in part to the antipyretic action of the drug, partly to the bacteriostatic effect. As a rule the earlier the sulfonamides are begun, the better the effect. The drug should be given in full therapeutic doses, it should be continued in full doses until all evidence of infection has disappeared, and it should then be continued in diminishing doses for another few days to prevent a recrudescence of the infection. With sulfonamides some acute otitis medias that otherwise would require a paracentesis or would rupture spontaneously clear up without a perforation of the drum membrane. When the bony changes of surgical (coalescent) mastoiditis are well advanced the sulfonamides are less likely to effect a spontaneous resolution of the infection, for with abscess function there is less chance of the drug reaching all the organisms. Certain organisms appear to be sulfonamide resistant. When the symptoms continue unaltered by the medication in full doses for three or four days, the organism is probably sulfonamide resistant and there is little advantage in continuing the drug. In cases of otitis media that fail to improve, and when there is the suspicion of a developing surgical mastoiditis, a lateral sinus phlebitis or a meningitis that is being masked by the drug, the medication should be discontinued for a few days until a diagnosis can be made and the appropriate surgical procedure determined. While the incidence of surgical mastoiditis and the complications of acute otitis media appear to have been definitely decreased by the sulfonamides, the drugs are not a substitute for surgical therapy when the indications for the latter are present.

CLASSIFICATION OF STREPTOCOCCI

To the Editor:—**Where can I obtain killed suspensions of various Lancefield types of streptococci for agglutination tests? The larger pharmaceutical manufacturers state that they do not have these suspensions available.**

M.D., Wash.

ANSWER.—It is difficult to obtain a clear conception of the classification of streptococci and methods used for its determination. There is no Lancefield agglutination test.

Streptococci are divided into groups designated as A, B, C and so on. This is Lancefield's classification and is based on the presence in the organism of a group specific carbohydrate called C antigen. Its presence is determined by a precipitin test using group specific serums and an extract of the unknown strain.

Practically all streptococci pathogenic for man fall into group A. This group has been further subdivided by Griffiths into some twenty-six types on the basis of an agglutination test done with type specific serums and an emulsion of the unknown strain. The types are numbered from 1 to 30, excluding types 7, 16, 20 and 21, which were later found not to be group A strains. There are, however, troublesome cross reactions which Lancefield has shown are frequently due to the fact that agglutination can be caused by either of two protein antigens present in the organism, the T antigen and the M antigen. Some streptococci have the T antigen of one type and the M antigen of another. Lancefield has therefore established her classification on the basis of a precipitin test using type specific anti M serums and a bacterial extract which contains only the M antigen. The numbering of the Lancefield types follows the Griffiths classification, and additional types have been added so that over forty are now recognized, at least provisionally.

The determination of the group of an unknown streptococcus is a simple procedure which can be done in any laboratory. Group specific serums for this purpose are sold by the Lederle Laboratories which include directions in each package. By this method streptococci of group A, which are potentially pathogenic, can be separated from the other groups, which are usually of no etiologic significance.

Typing serums for determination of the type of a group A strain, either by the Griffiths agglutination or the Lancefield precipitin methods, are not available commercially. Both methods have certain limitations, so that experience or training is necessary for trustworthy results. In neither of these methods are killed organisms used. Standard type strains for the Lancefield method can be obtained from Dr. Rebecca Lancefield, Rockefeller Institute, 66th Street and York Avenue, New York; strains of the Griffiths classification from Lieut. Comdr. Francis F. Schwentker at the same address.

KITCHEN AND HEATING STOVES AS POSSIBLE SOURCE OF LEAD POISONING

To the Editor:—**1. What is the likelihood of lead poisoning occurring in kitchen personnel from burning ordinary 80 octane motor vehicle gasoline in army gasoline kitchen ranges used indoors? Often four ranges are burning at one time. Unleaded or "white gas" usually is not available, and ethyl gas is used frequently. 2. What is the likelihood of lead poisoning resulting from the use of improvised stoves made from drums or 15 gallon cylindric cans heavily painted on the outside with red lead paint? They are usually used in small closed in rooms, are usually heated with gasoline by the gravity feed drip method, but sometimes with wood, and get very hot. I should appreciate receiving answers to the questions asked and I'm sure many others will also in overseas areas where it gets cold during the winter months, particularly in army air force units.**

Captain, M. C., A. U. S.

ANSWER.—1. There is apparently little danger in using the army gasoline kitchen field range, model of 1937. In this type of range the gasoline vapor passes through a hot tube which apparently effectively breaks down the lead tetraethyl so that the lead is removed. If ethyl gasoline is used, new filters should be put in and the fuel jets cleaned, and also the generator passages should be cleaned regularly.

2. If one uses an improvised stove made of drums or cans which are painted on the outside with red lead, one ought to be careful not to have it too hot. They ought not become red hot, for then some lead might vaporize and be a hazard. It would be safer to remove the red lead. Likewise ethyl gasoline ought not be used in such a makeshift arrangement, as the lead may well be liberated into small occupied spaces. There might

be some danger under those circumstances which ought to be avoided. If this method of heating is essential, arrangements should be made for good ventilation of the fumes from the fire and careful handling of the fire ashes, which would contain lead.

SPLENOMEGALY AND ANEMIA ASSOCIATED WITH SULFONAMIDE THERAPY

To the Editor:—Can you tell me if splenomegaly with severe anemia is a possible toxic manifestation of sulfonamide poisoning? A girl aged 7 became ill during the first part of July. A diagnosis of rheumatic fever was made, and the patient was treated quite extensively with sulfonamides. Treatment for rheumatic fever continued until September, when the patient was taken to my brother, who found an immense spleen and severe anemia. I first saw the patient in consultation with him; the spleen pretty well filled the left side of the abdomen, the red blood cell count was below 2 million and the white blood cell count was between 10,000 and 15,000, with picture said to be consistent with chronic leukemia. Blood transfusions revived the patient several times, but she recently died. The predominant picture throughout was the enlarged spleen and the severe anemia. The white blood cell count was never outside normal limits. Is there any possibility that the sulfonamides she took caused the fatal condition to develop? Is enlarged spleen ever a result of sulfonamide poisoning?

Melvin A. Drake, M.D., Buhl, Idaho.

ANSWER.—Splenomegaly and severe anemia may be caused by sulfonamide therapy. These findings have occurred in patients who have developed an acute hemolytic anemia as a result of sulfanilamide medication. Splenomegaly is not uncommonly associated with sulfathiazole therapy, and under these circumstances the splenic enlargement is usually only one of the manifestations of drug hypersensitivity. The patients usually have an associated fever and dermatitis. Anemia is not usually a pronounced finding. Unfortunately, as far as the present case is concerned, splenomegaly and severe anemia may be associated with acute rheumatic fever and also with chronic leukemia. From the data given, it would appear that the patient died because of chronic leukemia and not because of rheumatic fever. To date there is no reason to believe that sulfonamide therapy will cause leukemia, and no evidence has been offered in favor of this thesis. If the patient had unqualified evidence of leukemia as detected in the peripheral blood films, one can only conclude on the basis of present knowledge that the sulfonamide therapy did not play any part in its development.

SECRETORY PHASE OF ENDOMETRIUM AND OVULATION

To the Editor:—Does a lack of so-called secretory activity of the premenstrual endometrium always mean that ovulation has not taken place that month? How long before menstruation is it wise to take the endometrial biopsy for this test? Is four or five days before menstruation began too early for the secretory activity to show up on biopsy if ovulation has taken place? The statement is made by some that if a woman has primary dysmenorrhea it means that she has ovulated that month. Is this statement true?

M.D., Virginia.

ANSWER.—The typical secretory phase in the endometrium is usually indicative of ovulation. Although the endometrial pattern should be typical of the secretory phase four to five days before menstruation, it is well to postpone the endometrial biopsy until the onset of bleeding. This precludes the possibility of interfering with an early pregnancy. The cervical canal is more patulous at this time. Although functional dysmenorrhea is usually associated with an ovulatory cycle, its presence is not proof that ovulation has preceded menstruation. In the endocrine treatment of dysmenorrhea endometrial biopsies have revealed that ovulation can be followed by a relatively painless menstrual period.

DEVELOPMENT OF RH AGGLUTININS

To the Editor:—Assuming that an Rh negative woman is married to an Rh positive man, what would be the percentage probability that anti Rh isoagglutinins would be formed in her blood (1) in her first pregnancy and (2) in the second and subsequent pregnancies? Will the fetus necessarily have erythrobiastosis if the mother has anti Rh isoagglutinins in her blood?

Captain, M. C., A. U. S.

ANSWER.—The first two questions cannot be answered satisfactorily at this time. The variability of the factors concerned, e. g. variations in the permeability of the placenta, the occurrence of mild forms of erythroblastosis, the inheritance by the father of the Rh factor from both parents (homozygosis) or from only one (heterozygosis) prevent the determination of any reliable percentage probability at present. Experience does indicate that the development of anti Rh agglutinins in Rh negative women may increase with each pregnancy. The child of a mother with anti Rh agglutinins is not necessarily the subject of clinically recognizable erythroblastosis. Such cases have been observed.

PROBABLE ALLERGY TO TOPICAL MERCURIAL PREPARATIONS

To the Editor:—About three weeks ago I applied tincture of merthiolate 1:1,000 to a few minor scratches on my arms and legs. Shortly after an intensely itching dermatitis developed which does not seem to abate with various ointments and lotions. At first the dermatitis was confined to the sites of the original application of the merthiolate, but now it is spreading to other areas. I have used "Amertan" and "Merthiolate Cream" but the reaction resulted only in an intensification of the symptoms. Plainly I am allergic to or have an idiosyncrasy to merthiolate in any dilution or form. Please let me know of any medication I might use for the relief of this condition.

M.D., Connecticut.

ANSWER.—It is probable that the skin condition described is due to allergy to mercury, either newly acquired or more severe than had previously been present. This conclusion is based on the fact that merthiolate (an organic mercurial) is the common constituent of Tincture of Merthiolate, of Merthiolate Cream and of Amertan. The latter is a 5 per cent tannic acid ointment containing 1:5,000 merthiolate.

The treatment for this condition is, first, to eliminate all possible contact with any mercurial compound and, secondly, to use either protective or soothing applications, depending on the state of the lesions. During the acute phases of such a dermatitis, wet applications are usually most beneficial, i. e. cold saturated boric acid solution, diluted solution of aluminum acetate (Burow's solution) 1:20 to 1:10. After the acute phase, when the lesions are no longer weeping, itching and swollen, protective ointment may be used.

PIGMENTARY DEGENERATION OF RETINA OR RETINITIS PIGMENTOSA

To the Editor:—What is the present status of treatment of retinitis pigmentosa? Is nonspecific protein therapy worthy of a trial, and, if so, what material and dosage should one employ?

Alan A. Bassett, M.D., Little Current, Ont.

ANSWER.—Retinitis pigmentosa is improperly named, for the condition is one of degeneration, not inflammation, and hence should be called primary pigmentary degeneration of the retina. The term "primary" must be included to differentiate it from clinically similar pictures that ofttimes follow certain inflammatory conditions in the retina and choroid. In view of the basically degenerative character of the disease, it is obvious that therapeutic measures of the many types that have been tried, including foreign proteins, can have but little influence on the condition. In recent years endocrine therapy seems in many cases to have retarded the progress of the degeneration, but, to quote from Duke-Elder, "The clinical course is slow, chronic and progressive but is very frequently interrupted by remissions during which visual acuity and fields improve, a happening which has too often been interpreted as being a response to some particular line of treatment." Again, the same author said "In assessment of all of them [forms of treatment] it is well to take into consideration the natural fluctuations in the progress of the disease as well as the enthusiasm of the practitioner and the credulity or the desperate hopefulness of the patient."

NOCTURNAL CRAMPS IN THE LEGS

To the Editor:—In Queries and Minor Notes Feb. 12, 1944, page 471, Dr. T. H. Standlee of Mirando City, Texas, inquires about nocturnal cramps in the legs. Within the last few months I have had 3 patients with this condition, and I have tried every conceivable form of medication. I always thought it was akin to tetany. All 3 of my patients have been relieved, I hope permanently. They were given alkaline catharsis as small doses every morning of sodium phosphate, and before retiring they alternately placed each foot on the opposite thigh, sitting on a chair, thus relaxing it and passively manipulating all the toes and metacarpal joints and the ankle. They did this quite vigorously. This causes a local congestion and an increase of the blood supply in this area. It also stimulates the nerve endings here. I have spoken to a number of my medical friends about it and they have had similar good results. Occasionally a patient has spasms of the calf muscles; here too, when the muscle is relaxed, deep vigorous kneading should be of value.

Siegfried Block, M.D., Brooklyn.

THIAMINE HYDROCHLORIDE FOR CRAMPS IN LEGS

To the Editor:—In the answer to the question on "Nocturnal Cramps in Legs" in the February 12 issue I notice that no mention was made of the use of vitamin B_1 in this condition. I have become convinced that the use of sufficient amounts of this drug (10 to 30 mg. daily) will relieve the leg cramps not only in the pregnant but in the majority of other patients that have them, both old and young. However, it has to be administered parenterally in some cases to obtain proper results. Because of the unusually good results that are obtained from it, I believe that its use should be considered as almost specific. Few cases fail to respond with this treatment.

J. W. Carney, M.D., Logan, W. Va.